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THE EARLY FAILURE OF BREAST FEEDING

A CLINICAL STUDY OF ITS CAUSES AND THEIR PREVENTION

BY

HAROLD WALLER, M.B.

(From the British Hospital for Mothers and Babies, Woolwich)

'It would be of the greatest service to medicine if the determination became general to submit every minor problem of clinical work in which the conditions allow to methods by which an exact decision would be possible.' (Wilfred Trotter, Art and Science in Medicine.)

In the last fifty years, which have seen so much achieved in the protection of infant life, little has been added to our understanding of the unreliability of lactation; yet the key to this riddle would remove what is still the greatest risk surrounding the first weeks of life. In the attempt, which will be described here, to find part of the solution, lactation's common tendency to fail will be treated as a defect of the mammary gland and not, as is more usual, as arising primarily from faults in the conduct of breast feeding. This approach in no sense overlooks the importance of correct management but is adopted with the object of trying to define with greater clearness certain factors governing the maintenance of milk secretion. To separate physiological factors from the details of practical management may seem artificial, and it is not intended that the distinction should be rigidly binding. If the instruction given to women is to be helpful and, above all, if the teaching given to pupil midwives is to be of service to their patients, they should rest upon a sound physiological basis and find their confirmation in practice. It is doubtful if even the hardiest supporter of present-day teaching could advance this claim for its results.

As a broad generalization it may be said that women's experience of breast feeding is of two main kinds. In one there is from the outset no break in the continuity of a free and plentiful yield of milk. In the other the yield, though it may be plentiful enough at the start, declines or ceases completely within a few weeks: it may be even within a few days. This difference over-rides all others based on circumstances or social standing, and transcends in importance all the range of variation in human temperament and character which is so apt to occupy discussions on the prevalence of artificial feeding. There can be no doubt many women resume domestic work too early after delivery and need a longer convalescence; are over-burdened with family cares; are unskilled in infant management. Some are incapable of the discipline necessary to succeed in breast feeding and a few are frankly unwilling. Let it be granted also that failures arise from the lack of interest shown by doctors, from mistakes made by maternity nurses and health visitors; and, as is frequently emphasized, from the rigidity and bustle of hospital routine. To all these causes, at one time or another, I have attached a major importance. But after a closer study of the ways in which lactation starts it seems necessary to place above and apart from them all the breast's productive power and the ease with which milk flows into the baby's mouth. If these two conditions are present in full measure women will, as a rule, be found in the group who succeed; and they will succeed without skilled assistance and quite often with a cheerful disregard of the rules framed so carefully for their guidance. In the presence of factors which lower production or interfere with the free passage of milk from breast to baby, women commonly find the task more than they can accomplish. Although I believe this rough classification is substantially correct, I would repeat it is put forward mainly to focus attention on the functional properties of the breast.

The scarcity of statistics

Statistics of the duration of breast feeding are few and the causes of failure are seldom given in detail. A recent Government publication says 'Study of the figures leads us to estimate that about 80 per cent. of babies leave hospital wholly breast fed, and that 95 per cent. of the babies born on the district are wholly breast fed when the midwife leaves. Whether the infants are hospital or home born it appears that by the end of three months only some 50 per cent., and at the end of six months 40 per cent., have continued to be breast fed' (Ministry of Health, 1944). The greater number of initial successes among those confined at home is attributed to the higher number of uncomplicated deliveries and to these I would add the higher proportion of multiparous women. Primiparae succeed no better when delivered at home by midwives than in hospital. Finlay found in Edinburgh that only 55 per cent. of babies were being breast fed at the age of three months and McNeil (1940), contrasting

this number with the 80 per cent. which are wholly breast fed on leaving the Royal Maternity Hospital says: ' If these figures are applicable to all Scotland, it means that breast feeding, the ideal method of nutrition and the main bulwark against infection, is withdrawn in about 25,000 cases in these early months when the baby is specially vulnerable.' (In support of this it may be added that in a series of 48 infants under a year of age admitted to a ward for bronchitis or pneumonia, only five (10·4 per cent.) had been breast fed for more than seven weeks. There were six deaths in the series.) Closer enquiry would show that in the majority the change to artificial feeding is made far earlier than three months. Walker (1942) found that of 650 babies attending an infant welfare centre in Bournemouth 53 per cent. were breast fed for less than three months and 23 per cent. for less than two weeks. Robinson (1943), working in Liverpool, made a careful analysis of 1100 instances of weaning before the age of seven months and found that no less than 583 (53 per cent.) occurred within the first month. The most important item in this enquiry is that in 232 (40 per cent.) of these early failures she could discover no cause. ' About 40 per cent. of the women could give no reason for their failure to continue breast feeding and no reason could be found on examination; the breast milk had just " dried up " and resisted all efforts to increase it.'

In a group of 436 primiparous women seen consecutively at infant welfare centres in East London, it was found that 28 per cent. had ceased to breast feed by the end of one month, 38 per cent. before two months, and 42 per cent. before three months; the first two months thus covering almost the whole. Further, of those who failed soonest, 122 in number, almost all said their milk had ' left them ' when they got up or within a few days after. They mostly added that if they made the attempt to persevere ' the baby always seemed hungry,' that they ' could see it was not getting on,' and that its behaviour changed at once and it became ' satisfied ' when bottle feeds were given. Many knew their baby was considerably below its birth weight on leaving hospital; some were uneasy because the midwife had told them the birth weight or the weight at fourteen days, but not both, and they suspected a fall. Such statements may not always be strictly accurate, but it is unwise to disregard them or try to explain them away. Most of these women were seen in their homes by health visitors to whom they were well known, and were visited within two or three days of their return from hospital or of the end of the midwife's attendance; many were interviewed not much later at an infant welfare centre. In a large proportion their account was supported by the fact that their breasts had already regressed far towards complete involution. Yet, at the end of the lying-in period, their lactation had been entered as ' satisfactory ' on the report from hospital or midwife in 112 of the 122 (92 per cent.), and the babies as breast fed without the aid of supplementary milk. It was not possible to correlate failure in more than a few with ill-health, the strain of work, poverty, illegitimacy or any of the reasons usually held accountable. Indeed, apart from the change in the breasts, the women who failed differed in no particular from those who were feeding their babies without difficulty, and who had been confined in the same hospitals or were attended by the same midwives. In these women, as Robinson found in Liverpool, ' the breast milk had just dried up.' It becomes clear that at the end of the first fortnight ' wholly breast fed ' cannot be construed as ' securely breast fed.'

Here, surely, lies the heart of the problem; the liability of secretion to cease so soon after it has started. Some factor, it seems, has interfered with its maintenance ; interfered, because there was nothing to suggest that the majority had not produced milk during at least the first week. On the contrary, it was quite common to hear they had produced too much.

A somewhat more detailed enquiry was made into the events of the first fortnight by questions put to a series of 52 women on their first attendance at an infant welfare centre. Their answers bring out a close association between excessive milk secretion at the outset and a rapid subsequent decline, and with this also a high rate of damage to the nipples.

	Breast	Bottle
Type of feeding at 4 weeks..	22 (42 per cent.)	30 (47 per cent.)
Early milk plentiful	20	26
Overloading of the breasts	10	24
Relief attempted by breast-pump, etc.	6	21
Child unable to get milk easily	4	17
Injury to the nipples ..	8	22
Mastitis	0	3
Breast abscess	0	1

In this group, again, the reports from hospital and midwives were, with two exceptions, uniformly favourable, and no mention was made either of the difficulties which the women themselves described in getting their babies to feed or of the injury and pain they suffered in the process. Indeed, the terms in which many referred to the pain of suckling, when the nipples were damaged, suggested it might well have been a strong deterrent to continue feeding. For example, one young mother who contracted mastitis revealed that throughout two days she substituted a finger for the nipple each time the baby was brought her to feed, trusting the nurse to discover by test weighing that it obtained no milk. On the assumption that pain was a powerful source of discouragement I obtained the co-operation of the nursing staff at the British Hospital to institute an energetic campaign in the lying-in wards with the object of seeing whether this common complication could be prevented. Such conclusions as we reached on the influence of pain on secretion will be mentioned later. Meanwhile, this article will deal mainly with a number of points which arose as the work extended in directions not at first contemplated. They are described in detail not only

because of their bearing on the table set out above, but because they apply to the majority of failures occurring in the first weeks.

The prevention of injury

There are two main reasons why the nipples get damaged in the early days of breast feeding. One depends on its range of protraction and whether or not it is easily drawn away from the breast far into the baby's mouth. The other is the occurrence of engorgement of the breasts, which produces oedema involving not only the covering skin but the areola and the surface of the nipples. If suckling is allowed while the oedema is present a breach of the nipples' surface is inevitable. Here, again, the factor of deficient protraction enters, for the great swelling and tenseness of the breasts restrict the distance to which the nipples can be drawn out.

The first step therefore was to try to improve structural defects of the nipples and reduce engorgement whenever it arose. The former proved the easier task. A glass shield was employed with a central opening, a relic of Victorian days, designed originally to collect the overplus of milk and protect the nursing mother's clothing. Worn during pregnancy under a firm support it serves our purpose by pressing the nipple through the opening and gradually stretching and loosening its attachment to the deep structures of the breast. In all but the worst types of deformity the results are good. The length of time it needs to be worn depends on the degree of defect to be overcome, and for this reason the breasts should always be examined early in pregnancy. Usually it is enough if worn for the greater part of the day during the last three months, but some need it for longer. To ensure accuracy of position as well as for purposes of symmetry, two should be worn even if only one nipple is defective. Pressure must be firm to be effective but should not produce discomfort. Most women become accustomed to wearing the shields within a few days, and in many years' experience no ill effects whatever from their use have been seen. No other measure results in a fraction of the same improvement.

FIG. 1.—The effect of shields on inverted nipples.

The prevention and relief of engorgement of the breasts is a less simple matter and calls for more detailed discussion. I shall describe our attempts before synthetic preparations of oestrogen were available and later give some account of our experience of stilboestrol. We have, however, learned to attach so much importance to the manner in which lactation begins that, despite the familiarity of its general features, a somewhat detailed account is necessary to explain the method of management which has for several years become the routine in the hospital.

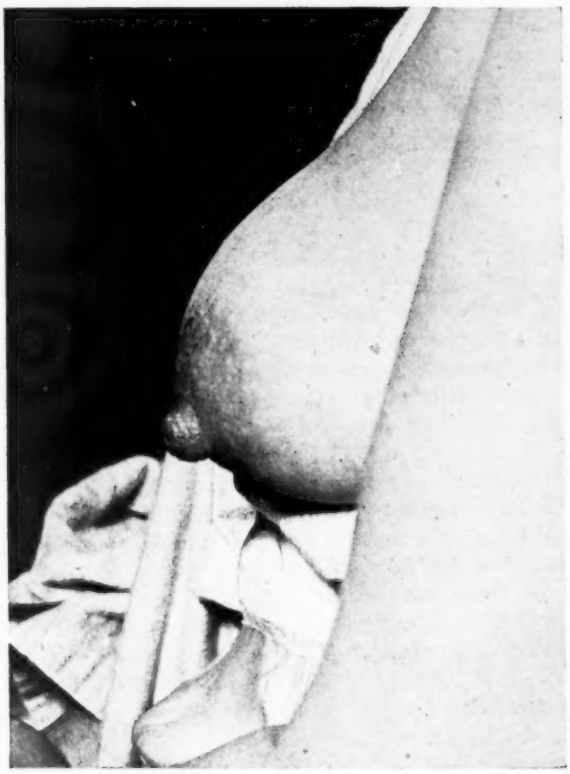

FIG. 2.—A nipple previously inverted and altered by wearing a shield during pregnancy.

The start of active milk secretion

If the changes which occur in the breasts as active secretion begins are watched, it is clear there are great individual differences in the rate and degree of filling and also in the freedom of the milk's outflow. In the first lactation the variety is so wide that its extremes present what amount to two distinct clinical types. There is first the type in whom neither enlargement of the breasts nor the tension within them becomes at all pronounced; filling is gradual and almost as soon as milk is formed it escapes from the nipples. This leakage is at first nearly continuous and by the combination of this and what the baby drinks tension remains low. These women suffer no discomfort. By about the tenth day both fullness and tension have come to

bear a distinct relation to the feeding interval; that is to say the breasts are full by the time the feed is due and comparatively lax when the child has fed. By this date, also, the spontaneous leakage has become intermittent, occurring at intervals of an hour or so. Next it becomes confined to the times when the child is suckled, milk flowing from one breast as the child feeds at the other. These changes represent the earliest signs of reflex outflow that can be distinguished, though as yet seldom forcible enough to evoke the clearly defined sensation to which women refer later as 'the draught' and which they describe as a tingling or 'pins and needles.' It is unusual for this to be realized earlier than the third week in the first lactation and is often delayed until later. By the tenth day a baby of average weight and vigour obtains from 15 to 20 ounces of milk in five or six feeds and has begun to regain the weight lost in the first days of life. The amount of milk rises steadily to 20 and 25 ounces daily and may reach 30 ounces by the end of the first month. This is the normal and favourable start of lactation and breast feeding may be expected to continue without let or hindrance. The figures at Woolwich place, as near as may be, 30 per cent. of primiparous women in this category.

In strongest contrast is a type in whom the onset of secretion is sudden or even violent, and if any leakage occurs at all it ceases within a few hours. Tension rises rapidly, the breasts become hot and heavy and enlarged to perhaps twice their former size, their margins standing out as a sharp ridge from the chest wall. The skin is tightly stretched and glistening, the veins full and prominent. During the next four or five days hard lobules of breast tissue may be felt, or sometimes seen, separately outlined; the state to which the term 'knotted' has been given. But by far the most striking fact is that not only does milk not escape spontaneously but that at the height of the engorgement it cannot be induced to do so by any of the means usually employed, and the baby's efforts to feed are wholly ineffectual. A variety of measures are used to induce the milk to flow; hot fomentations, icebags, the suction-pump and manual expression. But they produce little appreciable alteration, and for this reason many hold it is better not to interfere but rather to wait for the swelling and tension to subside spontaneously, as subside they will sometime during the second week. Meanwhile the woman experiences great discomfort, aching and sleeplessness to which, in a large proportion, is added the torture of suckling her child when her nipples are damaged.

For in addition to the signs just described the breasts are oedematous and pit on pressure. The oedema is often most easily seen in the thickened fleshy condition of the areola, while if the surface of the nipple is closely examined, preferably through a lens, it will be found to have a watery swollen look; and should the baby have been put to the breast there is added a pale yellow glaze, a lymphatic exudate. In the group to which this account applies we place 20 per cent. of primiparous women.

The two classes just described have no sharply defined limits and merging towards each are the remaining 50 per cent., showing every gradation of tension and ease of outflow. For clinical purposes it has been found helpful to distinguish four grades: the normal with tension scarcely raised; one with a moderate increase; the engorged state; and the last, just described, with oedema and obstructed outflow. A wider survey might show the number placed here at each end of the scale needs some modification, but the estimate is substantially correct. If the account and incidence of those in the last category are accepted it must be recognized that in a fifth of women at the beginning of the first lactation there occurs a period of excessively high tension lasting four or five days and sometimes longer. It is with the later course of lactation in these and their near neighbours in the third grade, perhaps another 15 per cent., that we shall be concerned.

High milk pressure. In veterinary medicine it has long been recognized that high milk tension lowers production and, if excessive and prolonged, suppresses it altogether. This sequence is seen in the human when the fœtus is stillborn. Milk is secreted after the usual interval and the breasts pass into the state of massive overload. After a few days production stops, tension becomes less, the milk is absorbed and regression to the resting stage soon follows. In hospital practice to-day it is rare to see the cycle completed, for secretion is artificially inhibited. Formerly the process was left to itself, except that to hasten it further pressure was often added from without by bandaging the breasts firmly to the chest wall. Even without this, involution was practically complete by the end of a fortnight, by which time the breasts were no larger, and were sometimes smaller, than before active secretion began. The same process is seen when the baby finds milk is easily withdrawn from one breast but not from the other. One can often see the change beginning in the unemptied breast during the lying-in period, but it has become much more conspicuous a few weeks later when the gland has shrunk to half, or perhaps less than half the size of the one which is taken. During the stage of extreme engorgement even the most vigorous infant is powerless to extract milk and will only damage the nipples very severely if allowed to try. Both facts, damage and impeded outflow, are due to the oedematous state of the breasts; for oedema which is evident in the covering skin must permeate the whole structure of the gland and involve the duct system. Thus, as regards drainage, the situation in no wise differs from that which follows stillbirth and the same tendency to involution is present. Discussing this relation between excessive tension and reduced production, Hammond (1936) says:

'There is some histological evidence whereby the increased milk pressure inhibits the rate of milk secretion and eventually leads to atrophy of the gland cells.

In the empty gland the space occupied by the alveolus is small and the cells are columnar, their natural shape in which they can best carry out their physiological process of milk production. But when the alveolus becomes filled with milk under pressure its diameter is doubled so that the individual cells have to expand if they are to remain intact, and they become flattened and drawn out. Neither this, nor the occlusion of the capillaries on the outer side of the alveolus by the milk pressure within is conducive to a high degree of activity in the mammary cell.'

Again, Dawson (1935), in a histological study of the changes seen in post lactation involution, says they occur in this order: '1. The acini become distended with retained secretion which may in places cause rupture of adjacent walls to form larger lumina. 2. This distension flattens the epithelial cells, inhibits the changes associated with secretion and gradually prevents its formation. Distension also causes interference with the capillary circulation surrounding the secreting acini and further favours epithelial inactivity and retrogression.'

Thus both these authorities agree in attributing the first step in the decline of production to alveolar distension. As a rider to the second quotation it can be added that weaning, when it is conducted gradually is not usually, accompanied by anything like the degree of raised milk pressure we are now discussing.

On theoretical grounds then there was much to suggest that whenever this state of overload arises, and for as long as it persists, secretion is endangered and the gland likely to revert to the resting stage. In medicine efficient emptying of the breasts has long been accepted as an essential factor in preserving the continuity of the yield, but in this situation withdrawal of milk by the baby is not possible. Among those of the 52 women in the table who failed so early the commonest statement was that the baby 'didn't seem able to get the milk out.' At the height of engorgement this is understandable, for outflow is actually obstructed. Normally by the second week the reflex expelling force has already come to the baby's assistance, and a week or two later will often reduce its task to little more than the act of swallowing (Waller, 1943). It seems probable that in women as in animals a necessary condition for this reflex is that milk pressure must be kept within a certain range; that it is not evoked below the lower limit and is inhibited if the upper limit is exceeded. The latter is much below the point at which oedema accumulates, so that it may be supposed production is threatened in many instances of severe but not extreme overload. And so, in fact, we found when following up patients after they left the hospital. On all grounds, therefore, and not only as a means to prevent injury, it seemed desirable that overload should be reduced as quickly as possible whenever it arose.

For fear of causing damage the use of any form of suction apparatus was ruled out of court, expression by hand being relied upon as more nearly representing the force by which milk normally leaves the breast. Applied to those with moderate

FIG. 3.—Manual relief of the breast by the mother herself. She learnt the method during pregnancy and was very skilful. The nipples were poorly developed and the lacteal sinuses apparently absent. Milk could only be expressed by pressure applied far back. The baby was weakly and was unable to obtain milk direct for a fortnight.

degrees of overload the benefit was immediately evident, for when tension was lowered the baby's intake rose at once and feeding was found to be secure when reviewed some weeks later. The method was at first thought to be inapplicable to extreme cases with obstructed outflow, but later, with practice and greater skill, several of the nursing staff were able to reduce oedema to the point at which some release of milk was obtained. To effect the necessary lowering of tension two hours of a

FIG. 4.—Relief of high milk tension by a nurse. Thumb and finger are compressing the lacteal sinuses. The funnel is a convenience in collecting the milk.

nurse's time might have to be given several times a day to one patient and when, as often happened, a number needed attention the ward work became disorganized. Again it was found that the yield was preserved in those in whom a free outflow had been quickly obtained, and declined or ceased when the task exceeded what the staff could manage. Some other plan had to be devised. An attempt was made to teach the patients themselves the technique of manual expression, but the time between delivery and the start of secretion was too short for them to acquire the necessary skill. It then appeared that this might be overcome by teaching them to express colostrum during the last weeks of pregnancy when time could be set aside to instruct them in greater detail. These stages are mentioned because the last had an entirely unexpected outcome, and on looking back it is recalled that it was embarked upon without any great hope of success. But the plan had only been in force a few months when the staff of the lying-in wards reported a notable reduction of engorgement among those who had received tuition, and gave it as their opinion that those who had been most successful in acquiring the technique hardly needed to apply it when lactation began. As time passed support for this view increased, the inference being that in some way the pre-natal removal of colostrum improved the subsequent outflow of milk.

It is known that in certain animals the regular removal of colostrum results in its replacement by milk before parturition. Had we, perhaps, produced some change comparable with this, such, for example, as a reduction in viscosity? This was suggested by many women reporting that after they had practised manual removal for a few weeks they found colostrum flowed freely, whereas at the start they could only express a few drops. Moreover, they often described it as becoming 'thinner' and 'more milky,' and so it appeared to be. Some months were therefore spent on an investigation into both the viscosity and protein distribution of the pre-natal and early post-natal secretions. A bomb which destroyed a large part of the hospital wrecked much of the equipment and brought the work to an end; but enough had been done to suggest the pre-natal removal of colostrum led to no systematic alterations in composition (Waller et al., 1941). Nevertheless the feeling persisted that the women benefited, and this in itself was of enough interest to submit to the test of a controlled clinical experiment.

The pre-natal removal of colostrum

We decided to confine the experiment to observations on the first lactation, and as the patients booked for admission to the hospital they were labelled alternately 'Pupils' and 'Controls.' The breasts were examined and a number of anatomical features were recorded, including any defects of the nipples. All who were thought likely to benefit by wearing the glass shields were supplied with them irrespective of which group they were in.

During the last three months of pregnancy the 'pupils' were taught the method of using their hands which had been found most effective in expressing milk, each one being required to demonstrate her proficiency at intervals of a few weeks so that any faults in her technique could be corrected. This teaching was the only difference made between the two groups, for in the lying-in wards both received identically the same management in respect of the relief of any overloading of the breasts that was called for, the prevention and treatment of injury to the nipples, the number of feeds their individual babies required, the use of supplementary milk, and so on. The need for scrupulous impartiality was impressed on the nursing staff, not only in the interests of the experiment but particularly on behalf of the infants. I am satisfied this object was achieved. The criteria by which it was decided the experiment should be judged were:

1. The freedom of the outflow of milk. To ensure this was not a matter of opinion it was thought best to show it as the amount taken daily by the two groups of babies.
2. The incidence of overfilling and engorgement of the breasts in each group of women.
3. The incidence of injury of the nipples.
4. The number of each group still breast feeding at three and six months.

The supervision of the experiment was given to one sister, who was made responsible for teaching the pupils and recording all details. It was planned to compare 200 pupils with 200 controls and we had in fact taught nearly that number of pupils; but the experiment was greatly interfered with by bombing and late in pregnancy many of the women decided to be confined in the provinces, while others sought safety by dispersal soon after delivery. In the hospital all the patients had often to be moved to shelters in the basement many times in the twenty-four hours, and this made regular and accurate test-weighing exceedingly difficult; much material had to be discarded as incomplete for this reason. The enquiry was therefore closed when data of 100 patients in each group were completed.

Before setting out the results a word is needed on the estimate of the different degrees of breast tension which is met with at the start of active milk secretion. There is no means of measuring it and so it amounts to a matter of clinical judgement based on experience. For some months before starting the experiment its assessment was practised using the appearance of the breasts, their tension to the sense of touch, the presence of oedema and the freedom of the milk's outflow. Four categories were finally settled:—

1. THE NORMAL. In these tension scarcely rose. Outflow was free and there was no necessity for the manual removal of milk.
2. OVERLOAD. Moderate overfilling with rise of tension, easily controlled by manual expression of the excess.
3. ENGORGEMENT. A greater degree, often producing oedema. Feeding was withheld until this had subsided, and when allowed was preceded by removal of the excess. After the child had fed it was usually necessary to empty the breasts further by hand.
4. ENGORGEMENT WITH OBSTRUCTION. The extreme type with no outflow. The breasts were raised and firmly supported, and no

attempt at feeding allowed. Emptying by hand was begun as soon as any outflow could be obtained, and when this became free and all trace of oedema had disappeared the child was allowed to feed. Excess of milk removed before and after feeds.

The results of the experiment will now be given. To the figures of the first test there are added for further comparison the daily amounts of milk taken by the babies of 100 multiparous women, in whom the start of breast feeding is usually far easier.

FIRST TEST

DAILY AMOUNTS OF MILK TAKEN DURING THE FIRST 13 DAYS OF LIFE BY THE BABIES OF 200 PRIMIPARAE (100 PUPILS, 100 CONTROLS), AND OF 100 MULTIPARAE. AMOUNTS IN OUNCES

DAY	1	2	3	4	5	6	7
P ..	0·1	1·0	3·9	8·7	11·7	13·6	15·3
C ..	0·0	0·7	2·7	6·6	10·0	12·4	13·4
M ..	0·3	1·3	4·4	9·0	10·8	12·8	14·3

	8	9	10	11	12	13
P	16·4	17·1	17·7	18·3	18·2	19·9
C	14·5	15·9	16·3	16·4	16·9	17·0
M	15·0	16·3	16·8	17·1	16·9	17·8

P = pupils. C = controls. M = multiparae.

SECOND TEST

MILK PRESSURE DURING THE FIRST DAYS OF SECRETION: 3RD TO 13TH DAYS

	Pupils	Controls
1. Normal	63	23
2. Overload	12	21
3. Engorgement	20	37
4. Engorgement with obstruction	5	19
	100	100

THIRD TEST

INCIDENCE OF INJURY TO ONE OR BOTH NIPPLES

Pupils .. 12 Controls .. 24

FOURTH TEST

SUCCESS OF BREAST FEEDING AT THREE AND SIX MONTHS; TO WHICH IS ADDED THE STAGE OF FEEDING ON DISCHARGE FROM HOSPITAL ON THE 14TH DAY

		WHOLLY BREAST FEEDING	PARTLY BREAST FEEDING	ARTIFICIAL FEEDING
On discharge	P ..	97	2	1
	C ..	83	12	5
At 3 months	P ..	87	2	11
	C ..	65	4	31
At 6 months	P ..	83	3	14
	C ..	42	5	53

P = pupils. C = controls.

The figures show very strikingly the correctness of the original observation by the hospital nursing staff. The first test revealed least clearly the true differences between the pupils and controls, for in the case of the controls' babies the amount of milk drunk from about the fourth to the eighth days often represents a combined total of what was taken by direct feeding and a residual quantity expressed and given by hand. This is the general practice in the hospital whenever it is necessary to ensure the breasts are sufficiently emptied, and it was a matter of general agreement that it was far more often required by the controls than by the pupils. Indeed any resistance to the pre-natal routine as an innovation disappeared as soon as it was realized how little help the pupils needed in getting their babies to feed satisfactorily and how, in consequence, work in the lying-in wards was lightened. The easy start of breast feeding by the pupils was likened by one of the sisters to that seen in the second or third lactation, and this suggested comparison with the amounts taken by the babies of a hundred multiparae. Most notable is the fact that in the quantity obtained the pupils' babies overtook those of the multiparae on the fifth day and never lost their lead.

But by far the most unexpected outcome of the experiment was the fact that 83 per cent. of the pupils were found to be relying wholly on breast feeding at the end of six months compared with 42 per cent. of the controls. This test was chosen to exclude the possibility of any temporary advantage to the pupils from encouragement derived from their training in the ante-natal period. It is not reasonable to suppose any such influence could have persisted for as long as six months after delivery. To what then can the greater security of their lactation be attributed? The explanation to be offered, though influenced by the findings given here, is based upon observations which cover a considerably larger field than that of this experiment and involves the discussion of a number of points not mentioned hitherto.

The conformation of the nipple and the terminal ducts

A first condition for satisfactory breast feeding is the ease with which the nipple can be drawn away from the breast so that it lies far back in the baby's mouth and rests between the base of the tongue and the soft palate. There its surface is protected from the force of suction which falls instead almost entirely upon the skin of the areola. Suction should draw the nipple into this position and maintain it there, bringing the lacteal sinuses within reach of the jaws so that their contents can be squeezed out by the action of the mandible, replenishment being brought about by the downward movement of milk taking place within the breasts. If at all resistant to traction the nipple tends to evade the baby's grasp or at the best will lie in the front of its mouth or between the lips. Here not only are the sinuses beyond reach but the nipple's surface is exposed to suction and is very quickly broken.

Gross types of malformation and inversion of the nipples are not likely to escape notice during pregnancy, but there is a large number which to casual inspection look well enough adapted to their purpose but which must be classed as defective if subjected to a careful test for the ease with which they can be drawn away from the breast. This test is not satisfied merely by pulling on them, for one is apt to apply more force than the baby is able to exert; instead it is necessary to observe what happens when, in imitation of the action of the baby's jaws, the areola is pinched just beyond the nipple's base. If this is done it will be found in a large number it causes the nipple to retract rather than to project. Those which react in this way are

too firmly attached to deep structures, and in some this attachment is felt as a hard cord which can be rolled between the fingers. This defect is a persistence of the original invagination of the mammary dimple which has failed to become detached when later it undergoes eversion. The so-called 'flat' nipple, which in many cases is under-developed rather than malformed and scarcely differs in structure from the areola, is usually quite lax and can be drawn far into the baby's mouth. Some, also, that appear wholly inverted can be turned inside out and present little hindrance to suckling. As already mentioned an attempt was made to detect all those with the least tendency to retract and to correct them before the birth of the child, for if left until then there ensues a contest between the child's strength and the nipple's resistance. A strong vigorous baby may succeed in effecting a grasp, but in process of doing so will almost always inflict damage; a less energetic one will only make perfunctory efforts and for this reason is apt to be labelled 'sleepy' or a 'bad feeder.' The notes made during pregnancy of the nipples' range of protraction when subjected to the test just described are as follows:

RANGE OF PROTRACTION OF THE NIPPLES (200 PRIMIGRAVIDAE)

	GOOD	MODERATE	POOR
Pupils.. ..	25	43	32
Controls ..	24	52	24

So high a proportion of defects is not likely to meet with ready acceptance, but it is scarcely open to question when sought for in the way mentioned. It receives support from the prevalence of another defect with which it is closely associated. The method of manual expression taught to the pupils consists of two separate movements. The first is a compression of the whole breast between the two hands, starting at its margins and continued down as far as the areola. Firm pressure is maintained throughout this movement, which is repeated ten or a dozen times. Its object is to impel colostrum from the finer into the larger ducts and the lacteal sinuses. The second movement is harder to acquire and is designed to empty the sinuses. Their position is found by trial and they are then pinched sharply and repeatedly between the thumb and forefinger of one hand while the breast is held firmly fixed by the other. This action should produce a flow of colostrum from the nipple, but success depends much upon the direction in which the force of the pinch is applied; it needs to be directed somewhat backwards towards the centre of the breast rather than towards the base of the nipple as is always the learner's tendency. But it depends also upon what I think must be the development of the sinuses themselves, both in respect of their size and position and probably of their number as well. In some women a very small amount of force produces a free jet of fluid from the duct openings, in others none or scarcely any. This is by no means related at all constantly to the amount of colostrum which the breast contains; for a quantity may be expelled by pressure applied to the whole gland when next to none can be obtained by the second manœuvre. Each pupil was taught how to get the best result in her own particular case, and when she had mastered the technique was instructed to carry out the exercise for ten minutes daily. In each an impression of the development and accessibility of the sinuses gained from this test was recorded.

DEVELOPMENT AND ACCESSIBILITY OF THE LACTEAL SINUSES

	GOOD	MODERATE	POOR
Pupils.. ..	30	43	27
Controls ..	31	44	25

The resemblance between these figures and those for the range of the nipple's protraction is very close.

A further point, though it is less certain how much importance should be attached to it, is the number of ducts which can be shown to open on the surface of the nipple by the time term is reached. It seems clear a large number of ducts must conduce to the ease and rapidity of the milk's outflow, and diagrams of the duct system always show such an arrangement. In fact, it is not so. The number may be anything from one to about twenty, and when single the opening is often at the bottom of a craterlike hollow or in the centre of a horizontal furrow.

NUMBER OF DUCTS PATENT DURING PREGNANCY

	NUMEROUS (10 or more)	MEDIUM (5 to 10)	FEW (1 to 5)
Pupils.. ..	32	21	47
Controls ..	26	24	50

The large number with a single opening and those with perhaps two or three caused us to follow them with particular interest, and we satisfied ourselves that in about half the entry in our notes had to be altered from 'single' or 'few' to 'several' before term was reached. In others the change was only discernible later and was recorded in the second week after delivery; but there are not a few in whom it is delayed still longer, a fact noticed by the women themselves and commented on as a point of interest. It is possible that this is related to the rise in the milk which the baby obtains as the days pass. It is hoped to take the subject of variation of the ducts and of sinus development further by photography with an opaque medium.

It remains to say a word about yet another anatomical detail which has a bearing on milk pressure. This concerns the capacity of the breast to expand as a whole; its elasticity in response to an increase in its contents. It is perhaps not usual to regard the breast as an encapsuled gland, but in fact the skin serves the function of a capsule and there are wide variations in its texture. The necessity for it to yield to pressure from within is seen in the striation which accompanies the laying down of glandular tissue during pregnancy. Stretching may show as deep red rents in the connective tissue when the skin is thick; as numerous, faint, radiating lines when it is more yielding; and is

not visible at all in the most elastic type. A simple way to gauge the differences is by choosing a place beyond the gland's margin, e.g. just beneath the clavicle will serve, and raising the skin between finger and thumb; here there is always some subcutaneous fat. When the test is transferred to the skin covering the breast the decrease in fat may be very striking; for here the skin can be more freely lifted up. In some it is as thin as tissue paper. But the change is by no means always present, and the transition from thick to thin may be absent altogether. In the experiment an attempt was made to record this point, but there was much less experience in making the test than any of the others. It has since been realized that the figures below should all have been given a decided shift to the right; that is to say, too many were classified as thin and too few as thick.

FIG. 5.—Illustrates thin elastic tissue covering the breast.

TEXTURE OF THE SKIN COVERING THE BREAST

	THIN	MEDIUM	THICK
Pupils.. ..	46	45	9
Controls ..	43	50	7

Even on this classification less than half had skin of the texture best suited to yield either to the enlargement in pregnancy or to the sudden increase in the breast's contents when active milk secretion begins.

The advantage of elasticity throughout the structure of the mammary gland has long been recognized in veterinary science, and has been one of the chief aims in the selective breeding of dairy cattle. Hammond (1936) states:

'The whole structure of the cow's udder appears to be designed for the relief of pressure on the secretory alveolar cells. The elastic fibrous tissue coat, the elastic fibres round the ducts and the thin elastic skin, producing an udder which "shrinks away to nothing" after the milk is withdrawn, or which will expand easily as milk is secreted into it—the ideal udder of the cattle judge—is a mechanism for keeping the internal pressure in the udder as low as possible compatible with the accommodation of a large volume of milk. The provision of a large milk cistern to each quarter, too, acts to relieve pressure on the actual secreting cells in the same way as the bladder acts for urinary secretion.'

So, too, in women the stretching which results from the first lactation serves to aid those which follow and largely accounts for the greater ease with which breast feeding is established in multiparous women. Since in them tension at the beginning less often reaches an excessive height, it gives us the explanation why reflex expulsion appears so much earlier, and why they tell us they can often recognize 'the draught' almost as soon as the milk 'comes in.'

The experiment was designed to test the observation that the regular removal of colostrum by manual expression appears to facilitate the subsequent outflow of milk, and it may claim to have done so. In each of the four tests selected the advantage lay with the 'pupils'; their babies obtained milk more readily in the first fortnight, they were less liable to engorgement and injury, and, as the follow-up reveals, the maintenance of their yield was secured twice as often as in the 'controls.' How can this result be related to the anatomical points we have been considering?

The reference to elasticity just quoted and to the existence in lower animals of 'cisterns' or reservoirs to safeguard the secreting cells, seems to give us a clue. These cisterns are represented in the human by the lacteal sinuses and these, it has been suggested, often appear to be poorly developed, a defect closely associated with a restricted range of the nipple's protraction. It has also been shown that the number of ducts patent at the nipple's surface at term is often small and may be single. In fact, it is not possible to examine a large series of women without reaching the conclusion that at the start of the first lactation the nipple and the terminal part of the duct system are ill adapted to their purpose in a high proportion. Thus, taking the three points just mentioned as being closely related to functional efficiency, in the notes of the 200 women in the experiment only 24 instances (11 pupils and 13 controls) are found of the presence in combination of free protraction, good sinus development and multiple duct openings; only 12 per cent., that is, with the ideal anatomical formation which ensures an easy task for the child and the best drainage of the breast. Even so this leaves out of account the quality of elasticity. The tendency to retraction can be overcome, or at least much improved, in many by the timely use of a simple apparatus, thus greatly aiding the child in its early efforts to feed or, it may be, providing the

only possibility of it feeding at all. But this by itself is not enough. It was supplied impartially to pupils and controls alike and the benefit derived was equal in the two groups; for, as would be expected, the incidence of abnormalities and their degree were almost identical in each. It is when the number subject to high milk pressure is compared that the groups part company, for 56 controls fall into the two highest grades of engorgement as against 25 pupils. This difference represents the difference in freedom of the milk's outflow, and the lower incidence among the pupils must be due to the pre-natal removal of colostrum having forced open and stretched the ducts in the lower part of their course before the inrush of milk which characterizes the action of the lactogenic hormone. In support of this is not only the greater amount of milk obtained by the pupils' babies in the first days of life but also the far greater ease with which their breast feeding began. There was a further fact which deserves a brief mention. The security of breast feeding depends closely on the delicate mechanism of the 'draught' reflex and its conditioning to the stimulus of suckling; and also to a degree of milk pressure which safeguards the secreting cells. The earlier this adaptation occurs the safer the outlook. Women vary much in their awareness of this expelling reflex, especially in the first lactation. In the follow-up, and before three months had elapsed, both groups used in the experiment were asked to state as nearly as they were able when they first clearly distinguished the sensation of 'pins and needles' which accompanied the draught. Not all the 84 pupils and 64 controls who were still wholly breast feeding their babies gave exact answers. For those who did the average was 3½ weeks for pupils and 4½ weeks for controls.

It has been suggested that the oil used on the hands to prevent friction in the pre-natal 'massage' of the breasts increases the elasticity of the covering skin and so enables it to yield more readily when the milk first 'comes in.' Any such effect is probably so slight as to be negligible. To avoid misunderstanding it is perhaps wiser to use some word such as 'preparation' rather than massage since the latter term has, in this connection, become endowed with almost transcendental properties of 'toning up' and 'stimulating' the gland to prodigies of secretion, whereas it is implicit throughout this discussion that it is an initial excess of milk production and its rapid drainage with which we have been concerned. It is more likely that the effect is mechanical and is produced in the way described. The method has also been called new, but any claim to novelty is better waived. I am informed it is met with in China and in some parts of Africa, and an account of what seems to be the same custom among the Maoris runs as follows:

'In the old days the breasts were massaged, and also the nipples, and a Maori mother never had the difficulty of the women who have come in contact with civilization. When a woman became pregnant her breasts were attended to from three months after (conception) right up to the birth of her child. Her breasts would have the milk flowing easily, and so the child is fed from them soon after birth.'

It will be remembered the work reported here began with the attempt to prevent injury, on the supposition that when the surface of the nipples is broken pain might well lead to a refusal to continue breast feeding. No conclusion has been reached how often artificial feeding provides an escape from pain. A rule of the lying-in wards is that the nurses must ask their patients at every feed whether the act of suckling causes pain, and to report each instance. The nipples are then examined with a lens and, if any breach of their surface is found, feeding is suspended until healing is secure; milk is taken off by hand at each feeding time and given to the baby by bottle. The problem of pain thus scarcely arises. Nearly all the cases of damage recorded in the 200 primiparae were of this slight degree and, judged by some standards, would not be considered injuries at all. The plan is amply rewarded for the deep fissures and denuded areas of former days are never seen, and mastitis or breast abscesses are almost negligible. (Another hospital maxim is that 'Every damaged nipple is a potential breast abscess.') So far as it has been possible to trace, among the 10,000 patients who have passed through the wards during the last nine years, there have been four abscesses. One occurred towards the end of pregnancy and coincided with the intra-uterine death of the fœtus; it was probably due to a blood infection from an antral empyema. The other three occurred within three weeks of the patients leaving and are accepted as the hospital's responsibility.

Injury carries a special risk of infection at this stage, when drainage is so often less free than it becomes a few weeks later. But the pain involved has also a special significance; its inhibiting influence on the expelling reflex. A woman may endure pain with the greatest fortitude, but it is doubtful if she can equally control its effect on reflex action. There is evidence that she cannot in the small amount a baby will obtain if allowed to feed when the nipples are damaged. Yet, as has been seen many times, the yield will rise at once if feeding is stopped and milk is regularly removed by hand. So, too, in animals, the milk is not 'let down' if they are hurt in the process of milking, or if they are frightened. It is beyond question that when suckling hurts, many women are extremely apprehensive of developing a breast abscess and will sometimes mention this fear only after all occasion for it has passed. Some are doubtless glad to give up the attempt to feed in the hope that it will lessen this risk; more often they will persevere in the interest of the child. One instance of the severity of the pain has been mentioned and another may be recorded. A young woman told me that while struggling to give her baby the breast when her nipples were torn, she was rebuked for letting her tears fall on its face. 'But I was not crying at all,' she asserted, 'it was sweat

dripping off my forehead.' In such circumstances it is impossible to suppose the breasts are efficiently emptied, and the decline which so often follows is probably due to this cause.

Owing to war conditions much of the work reported here has throughout its course been denied the benefit of discussion and criticism, and it needs some courage to suggest its conclusions are worth verification by others. Nevertheless, I hope it may be thought to be so. If the views propounded here are endorsed by trials elsewhere it follows that, to a far greater degree than hitherto, those in charge of the lying-in period must shoulder responsibility for the fact that nearly 50 per cent. of babies are deprived of human milk before they are three months old ; or even, as there is reason to think, before they are six weeks old. The training of midwives and health visitors in the prevention of high milk pressure must be a charge on the teaching staffs of maternity hospitals and must be directed by the obstetricians or the paediatricians whom they appoint to do it for them. Should it take the form advocated here, and now the routine at the British Hospital, it calls for some re-organization of the ante-natal clinic and I have been fortunate in being given every facility in effecting the change. Elsewhere it is possible some prejudice may have to be overcome. The recent Government Report ' On the breast feeding of Infants ' opens its discussion on why feeding is not established in so many women by emphasizing an ' over-sophisticated outlook on life,' and in some ' a distaste for the process which may be pathological in origin and sometimes impossible to overcome.' This is, of course, the customary approach to the subject which would scarcely call for comment; but it proceeds:

' It seems to us, however, that in some cases this distaste may have been engendered by an unnecessarily elaborate routine during the ante-natal period. We understand, and fully appreciate, that various forms of treatment may be required for various conditions and types of breast. Nevertheless we feel that if anything more usual than normal hygiene is required it should be prescribed by a nurse or a doctor, after skilled examination. It is, we fear, bordering on the paradoxical to impress upon the ordinary expectant mother that breast feeding is a normal, easy and natural process if at the same time the advice she receives as a routine imposes upon her an elaborate daily ritual of preparation. We think it possible that with an anxious type of woman too much stress on preparation of the breasts may alarm and discourage her to such an extent that she will refuse even to initiate breast feeding.'

It will have been evident that the whole tenor of this paper is throughout frankly opposed to the view that it is fair ' to impress upon the ordinary expectant mother that breast feeding is a normal, easy and natural process,' least of all in her first and most critical lactation. The paradox, surely, lies in the continual bolstering up of this misleading doctrine, so contrary to experience, so fruitful of error and disappointment. For perhaps 30 per cent of primiparous women it may hold good; for another 50 per cent. breast feeding is beset in varying degree by obstacles, many of which are hard to overcome; while for the remaining 20 per cent. it calls for all the skilled assistance which can be brought to it and even so will by no means always succeed. I am convinced no real improvement will be seen until these figures, or something approaching them, are frankly faced.

At the British Hospital for several years we have been teaching exactly what this Report condemns, and practically without exception it has met with a ready and eager response from the patients. Instruction is of course given by a doctor or nurse and is always preceded by a careful examination. The ' anxious type of woman ' who is supposed to be deterred from making the attempt to feed her child has, on the contrary, provided us with many of our most outstanding successes ; for as she masters the technique and appreciates its objects she almost invariably gains in confidence and composure. The same applies to those who in a previous lactation have suffered the misery of cracked nipples, of mastitis or a breast abscess. In the experiment described care had to be taken that the controls did not make trial of the pre-natal exercises through hearing of their reputation for giving good results. When giving demonstrations of the method at other hospitals and conferences a number of expectant mothers willingly agreed to go and act as exhibits (even as far from Woolwich as the Midlands) and show the exercises to large audiences of midwives and health visitors and before doctors and medical students of both sexes. The warning issued by the authors of the Report can be dismissed as groundless if it is desired to test the ' ritual ' and if instruction is in responsible hands.

It was stated at the outset that one of the puzzling aspects of breast feeding is its tendency to fail in some women, its effortless performance by others. The main grounds of difference put forward have been the hindrances due to anatomical defects and their bearing upon the physiology of milk secretion. There is, however, one more which needs at least brief mention. The contribution to successful drainage of the breasts by the child is a variable factor, and, whenever this is lessened by prematurity, by the stress of labour, the lethargy of jaundice, illness or other like factor a threat to the maintenance of lactation arises. The daily increases in the amount of milk taken by the child which is normally characteristic of its performance in the second week may be delayed considerably beyond this point, and, unless this is realized and due care is taken to control the level of milk pressure by adequate drainage, failure is likely for the reasons already given. Here, again, the phrase ' wholly breast fed ' on leaving hospital at the end of the customary lying-in period may denote no more than that the child is still being put to breasts which are rapidly reverting to the resting stage. It needs but a few more days for the mother to realize this, and the artificial feeding to which, quite rationally,

she resorts is attributed to unwillingness to breast feed. This explanation seems to have been accepted by those responsible for the Government Report. 'Many hospitals, we heard, had found mothers so reluctant to continue breast feeding that women who had left hospital completely breast feeding would turn up at the clinic a month later with their babies wholly artificially fed.' This is so entirely at variance with my experience of the cause of failure at the British Hospital and elsewhere over many years that I feel sure it does not do justice to the women and that a clearer understanding of the underlying physiology would provide a truer explanation. In a proportion of first-born infants, and it is probably not less than 20 per cent., the safe establishment of breast feeding is not feasible within the time usually allotted to the lying-in period ; yet it is in the maternity hospital that the foundations of security must be laid. The practice of discharging a woman merely with injunctions to keep to some timetable of feeding quite often results in her obtaining admission for her baby to the children's ward of another hospital a few days later, where she is ordered to attend herself to feed it. This can seldom avail. I have seen it done at a teaching hospital when it involved the mother in nine hours' travelling daily and at cost to her of over four shillings a day. Provision for a longer stay where she is confined and a far closer liaison between the nursing staff of the maternity hospital and the health visitors of its neighbourhood, are the most pressing needs.

The use of stilboestrol to control high milk pressure

In the prevention and reduction of engorgement stilboestrol has a useful field, but it needs judgement to adapt the dosage to the individual case. Enough should be given to reduce tension quickly and to confine the use of the drug to a short period. If engorgement is foreseen—and the staff has become very expert in its anticipation—two or three doses of 5 mgm., given by mouth at intervals of four hours may be all that is needed. With an exceptionally rapid and unforeseen rise of pressure it may be necessary to give 20 mgm. three times, followed by 15 and then by 10 mgm. at four-hourly intervals, and the dosage must not be allowed to lapse during the night. This amount produces a halt in secretion followed by a marked reduction of tension and relief to the patient but, as the effects wear off, a return of secretion is always seen ; this time it is gradual, so that for several days the baby may obtain very little and must be supplied from other women's abundance. As soon as swelling and oedema show signs of subsiding as the result of the drug the milk the breasts contain should be expressed by hand even though the amount is small. This is found to remove all risk of involution. Feeding is resumed as soon as any revival of secretion is detected. The after course of lactation is unaffected and the normal yield can be expected by the tenth or twelfth day. No ill effects have been seen either immediate or remote, and in following up women treated in this way breast feeding has been found to have gone on smoothly and securely, and after doses even higher than those described. In acute mastitis equally large amounts are called for, and can alternate with one of the sulphonamides, sulphathiazole in our experience being the one of choice.

Summary

The main principle put forward is that an easy start of breast feeding depends on milk pressure within the breasts not rising to an excessive height. If it does so rise, and if it is not speedily lowered, a rapid decline in production follows by reason of alveolar distension and compression of the secreting cells. This is claimed to be the chief reason for the statement by so many women that their milk fails soon after they get up from childbed. The frequency of high milk pressure at the outset of the first lactation is attributed to certain anatomical defects of the nipples and the terminal ducts, a claim for which there is ample clinical evidence but which needs confirmation by other and more exact means.

A controlled experiment is described in which half the women used were taught the daily removal of colostrum during the last three months of pregnancy, and their breast feeding compared with that of the other half who were not so taught, both groups receiving identical management during the lying-in period. Excessive milk pressure occurred in 25 per cent. of the 'pupils' and in 56 per cent. of the controls, while at the end of six months 83 per cent. of the former were still successfully breast feeding as against 42 per cent. of the latter. For this result it is suggested that the preliminary removal of colostrum facilitated the initial outflow of milk by stretching and enlarging the terminal part of the duct system. A simple means to improve the nipple's range of protraction is also described.

POSTSCRIPT. Since the experiment described here, the preparatory technique has as far as possible been taught to all primigravidae and those who have had experience of lactation difficulties. Replies to a questionnaire sent to 300 primiparae delivered consecutively in the early months of 1945 show that 79·3 per cent. were fully breast feeding at six months. In 5 per cent of this series stilboestrol was used as here described to control milk tension.

I wish to thank the Editor of 'The Nursing Mirror' for permission to reproduce the photographs.

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SOME OBSERVATIONS ON PENICILLIN

ITS DOSAGE AND ADMINISTRATION IN INFANCY*

BY

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These observations are based on a series of seventy-eight cases, under the age of one year, treated at the Hospital for Sick Children, Great Ormond Street. Thirty-seven of these infants were neonates (under the age of one month).

Prior to penicillin treatment, blood cultures, post-nasal swabs, rectal swabs, and swabs from any obvious site of infection were taken. Analysing the bacteriological results the predominance of Staphylococcus aureus as the causative micro-organism was striking. Infections with gram-negative bacilli were, of course, not included in this group, since they are not susceptible to penicillin treatment.

TABLE 1

MICRO-ORGANISMS ISOLATED FROM 78 INFANTS UNDER ONE YEAR PRIOR TO PENICILLIN TREATMENT

Staphylococcus Aureus ..	59 cases: 75 per cent. (14 per cent. with other organisms).
Haemolytic Streptococcus ..	18 cases: 23 per cent. (10 per cent. with other organisms.)
Pneumococcus	11 cases: 14 per cent. (6 per cent. with other organisms.)
Staphylococcus Albus ..	2 cases.
Klebs Loeffler Bacillus ..	1 case.

TABLE 2

(SUB-GROUP OF TABLE 1)

MICRO-ORGANISMS ISOLATED FROM 37 NEONATES UNDER ONE MONTH PRIOR TO PENICILLIN TREATMENT

Staphylococcus Aureus ..	30 cases: 81 per cent. (13 per cent. with other organisms.)
Haemolytic Streptococcus ..	11 cases: 30 per cent. (16 per cent. with other organisms.)

It is also worthy of note that in a series of twenty-five cases of bacteriaemia, Staphylococcus Aureus was isolated from the bloodstream in nineteen instances (76 per cent.).

This very high incidence of Staphylococcal infections constitutes a marked change of the predominant bacteriological flora compared with such statistics as are available of former years. Has a decade of sulphonamides pushed the highly sensitive organisms, such as haemolytic streptococci and pneumococci into the background, whereas it has but slightly touched the Staphylococcus aureus?

Since penicillin is much more powerful in its action on Staphylococcus aureus than even the most active sulphonamide (Sulphathiazole) its place in infantile infections appears to be established eo ipso.

Dosage and administration. The problem of dosage is not yet finally solved. As a practical suggestion, however, a dosage scheme of 1000 units per pound expected body weight per 24 hours is recommended, the expected body weight being calculated from the birth weight and age. A convenient figure near the calculated 24-hour requirement is made up in normal saline to contain one dose in 1 c.c. Injections are given every four hours intramuscularly, coinciding where possible with feeding times. Intermittent dosage has been found superior to a continuous intramuscular drip, since the risk of secondary infections by excreta is thus at a minimum.

Because of its rapid excretion by the kidneys, penicillin is usually given three-hourly. Impaired renal function leads to prolonged retention of penicillin in the body. Since renal function is not fully established in infancy, four-hourly spacing of injections is suggested. Similarly six-hourly injections in premature infants were tried and found to be quite satisfactory.

In trying to justify this proposed dosage scheme, penicillin levels were assessed in blood serum taken at varying intervals of the four-hour period between two injections.

Thirty-six serum samples of four infants were assessed for their penicillin content, first on the basis of 1000 units per pound body weight, and then of 3000 units per pound body weight. Estimations were made at half an hour, one hour, two, three and four hours after injections. The average results are set out in the following figure (Fig. 1).

In the adult, 1000 units per pound body weight correspond to a total of 160,000 units per 24 hours, or 20,000 units three-hourly, and 3000 units per pound body weight to 60,000 units three-hourly.

* Paper read at the British Paediatric Association Meeting, Rugby, August, 1945.

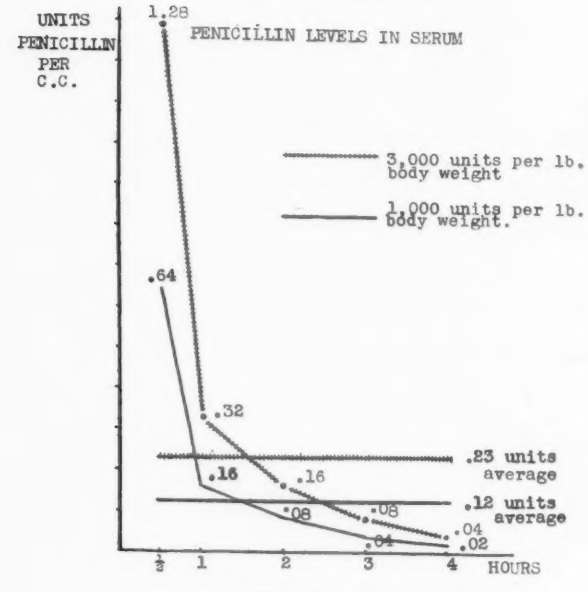

FIG. 1.

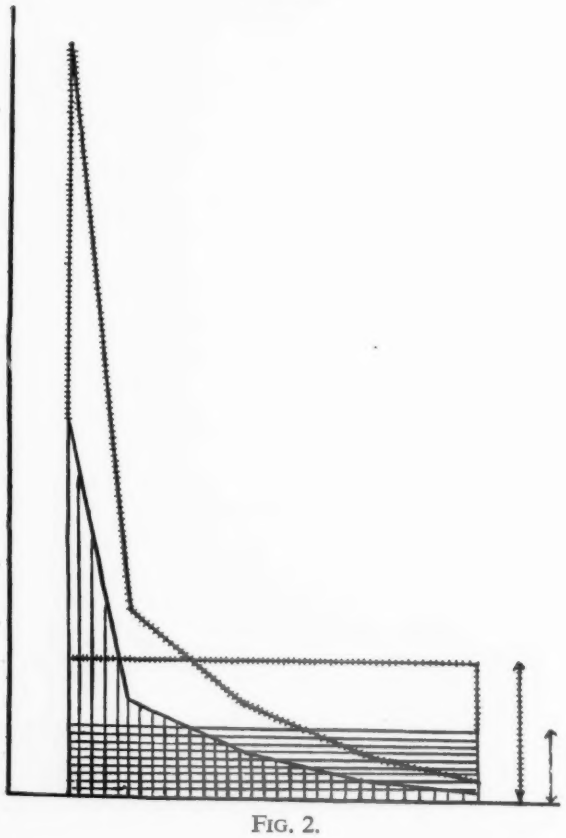

FIG. 2.

TABLE 3

AVERAGE PENICILLIN LEVELS IN SERUM

	Adults, 3-hourly	Infants, 4-hourly
1000 units per lb. body weight.	0·09 units/c.c.	0·12 units/c.c.
3000 units per lb. body weight.	0·21 units/c.c.	0·23 units/c.c.

Hudson et al. (1945) have compiled graphs on the 20,000 and 60,000 units basis. They also worked out a so-called 'average level.' The total surface area of the vertically shaded curve equals a rectangle (shaded horizontally) whose ordinate indicates the 'average level' (Fig. 2).

There is a close similarity in the 'average levels' in adults on three-hourly and in infants on four-hourly dosage (see Table 3). This would appear to support the wider spacing of injections in infants.

More penicillin levels were estimated at the latter period of the four-hour interval, i.e. three and four hours after an injection, in order further to justify the proposed four-hourly administration. These investigations were carried out on sixty-one infants, on 1000 units per pound body weight per 24 hours (Table 4).

0·02 units per c.c. appears to be the minimal effective level since it just inhibits the Oxford standard strain of Staphylococcus aureus as well as the standard haemolytic streptococcus which has been used in some of these estimations. It is worthy of note that 33 per cent. at four hours and 18 per cent. at three hours fell below 0·02 units per c.c. This, however, has not affected their rate of clinical and bacteriological recovery, compared with the infants in whom the levels were adequate throughout.

TABLE 4

PENICILLIN LEVELS IN SERUM ON THE DOSAGE OF 1000 UNITS PER POUND BODY WEIGHT

	Units per c.c.	No. of cases	Per cent.
At 3 hours after injection.	0·16	5	8
	0·08	9	15
	0·04	15	25
	0·02	21	34
	less than 0·02	11	18
This gives an average of 0·04 units at three hours.			
At 4 hours after injection.	0·16	2	3
	0·08	2	3
	0·04	7	11
	0·02	30	50
	less than 0·02	20	33
This gives an average of 0·02 units at four hours.			

Finally, further evidence in support of the proposed dosage scheme was adduced by an analysis of the sensitivity to penicillin of 123 strains of micro-organisms, isolated from cases in this series (Table 5).

It would appear that 86 per cent. of the strains analysed below are sensitive to the 'average penicillin level' of 0·12 units per c.c. obtained on the 1000 units per pound body weight basis. Only one case died in each of the 'less sensitive' and 'relatively insensitive' groups although treated on the same dosage; 3000 units per pound body weight

would but slightly affect the issue so far as penicillin-sensitivity is concerned. It would not cover the 'relatively insensitive group' if the 'average penicillin level' of 0·23 units per c.c. be taken as an indication.

TABLE 5

PENICILLIN SENSITIVITY TESTS ON 123 BACTERIAL STRAINS

Staphylococcus Aureus	86 strains
Haemolytic Streptococcus	20 strains
Pneumococcus	8 strains
Staphylococcus Albus	7 strains
Meningococcus	1 strain
Klebs Loeffler Bacillus	1 strain

GROUP I	GROUP II	GROUP III
Sensitive	Less sensitive	Relatively insensitive
(Inhibited by less than 0·1 units per c.c.).	(Inhibited by 0·2 not by 0·1 units per c.c.).	(Not inhibited by 1·0 unit per c.c.).
106 strains or 86 per cent.	7 strains or 5·7 per cent.	10 strains or 8·3 per cent.

Factors other than the penicillin-sensitivity of micro-organisms, however, might have an important bearing on the question of higher dosage in certain cases. These problems are still under investigation.

Discussion and summary

A bacteriological survey of a group of seventy-eight infants selected for penicillin treatment yielded Straphylococcus aureus in 75 per cent., in 81 per cent. of thirty-seven neonates, and in 76 per cent. of twenty-five cases of septicaemia.

A dosage scheme of 1000 units per pound expected body weight per 24 hours is suggested. This is divided into six doses and each dose made up in 1 c.c. normal saline, given every four hours intramuscularly.

Average penicillin levels on this four-hourly dosage scheme were compared with those in adults on a comparable dosage given at three-hourly intervals, and similar results obtained.

Levels were assessed three and four hours after an injection; they were still bacteriostatic in the majority of cases.

Eighty-six per cent. of all bacteria other than gram-negative bacilli tested for penicillin-sensitivity were susceptible to the average penicillin level obtained with this dosage. Three-fold increase of dosage did not affect the issue materially.

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AEROSOL PENICILLIN IN THE OXYGEN TENT

BY

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Penicillin is readily absorbed through the lungs when its solution in saline or water is inspired in the form of an ' aerosol ' mist from a closed inhaler (Barach et al., 1945; Mutch and Rewell, 1945) or even when dispersed into the atmosphere of a small room (Knott and Clark, 1945). Bacteriostatic concentrations in both blood and urine can be attained. Good therapeutic effects, particularly in respiratory tract infections, have been described (Vermilye, 1945). We have therefore made observations upon the absorption of penicillin by children in oxygen tents into which the aerosol was being discharged continuously. If a satisfactory blood and tissue concentration could be maintained the method promised the advantage that in children with severe bronchial or pulmonary infections and too young or too ill to tolerate any form of closed inhaler there would, without any disturbance of the patient, also be continuous direct application of penicillin to the infected areas.

From previous experiment we knew that atmosphere with relatively high concentration of penicillin aerosol could be inhaled for considerable periods without discomfort or after-effects of any kind. It was possible to remain for an hour or more in a small room visibly misty with aerosol and yet, after the first few moments, be virtually unaware of its presence. By collecting known volumes and bringing them into contact with small measured amounts of cold water of which the penicillin content was subsequently estimated, we found that these well-tolerated atmospheres carried as much as 35 units per litre.

It was therefore decided to devise some simple form of aerosol generator which, driven by pressure from an oxygen cylinder, would steadily discharge the mist into an ordinary oxygen tent. The apparatus had to fix firmly to the frame of the cot or bed, be of stout unbreakable construction, capable of working continuously for several hours, easy to clean and simple to re-fill. The generator which, with the makers' assistance, was finally developed and used in these experiments is illustrated in figs. 1 and 2.

Except for the thick glass penicillin reservoir at the base, the generator is of all-metal construction. The internal jet, the baffle plate and metal ducts are easily cleaned with water and can be sterilized when necessary. The glass reservoir has the advantage that consumption of the penicillin solution is easily watched. But in ward practice we found that all-

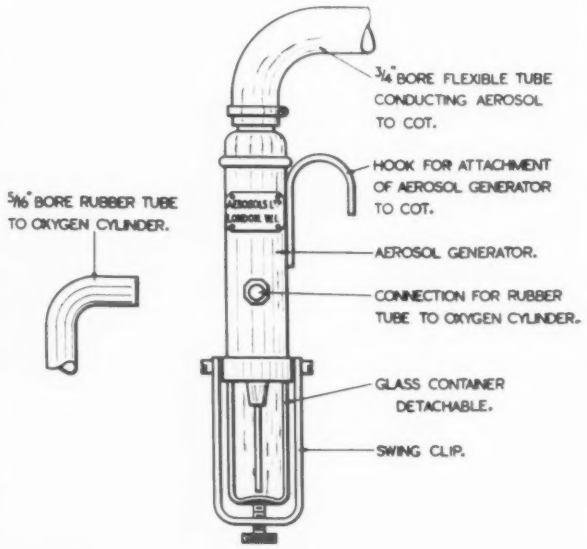
3/4" BORE FLEXIBLE TUBE CONDUCTING AEROSOL TO COT.
HOOK FOR ATTACHMENT OF AEROSOL GENERATOR TO COT.
5/16" BORE RUBBER TUBE TO OXYGEN CYLINDER.
AEROSOL GENERATOR.
CONNECTION FOR RUBBER TUBE TO OXYGEN CYLINDER.
GLASS CONTAINER DETACHABLE.
SWING CLIP.

FIG. 1.

FIG. 2.

glass jets were too frequently broken during cleaning. Rubber tubes of appropriate bore connect the generator with the oxygen cylinder and one of the lateral openings in the tent. At the end of the wide delivery tube is a short string leading to a spring clip which, attached inside to the fabric of the tent, lightly holds it in any desired position. In all our tests the medium size tents supplied by Oxygenaire Ltd. were used and their volume as set up averaged approximately 5,500 litres. Two oxygen cylinders were always used, one to operate the tent in the usual way, but, in view of the additional oxygen coming through the generator, we adopted the rather low rate of flow of about 4 litres per minute. The other cylinder was run at whatever rate produced a steady, easily visible stream of mist from the delivery tube. This flow was usually also about 3 to 4 litres per minute. If only one cylinder is available the flow can be divided by a Y-piece with a flow-meter attached to each arm, but in practice we found it preferable always to use separate cylinders. Ventilation control was then much better.

The penicillin solution placed in the generator contained 20,000 to 25,000 units per ml. in sterile normal saline. For cases 1 to 3 calcium penicillin was used, but in the remaining tests only the sodium salt was available. Some of the observers already quoted describe the calcium salt as producing the better aerosol, but we cannot pronounce on this point. Both were quite effective for our purpose. At the above rate of flow from the cylinder, 4 to 5 ml. of the solution are dispersed as aerosol within the tent per hour. With the ventilation flow mentioned, the atmosphere within the tent contained 15 to 20 units of penicillin per litre. The content of the air actually inspired may often have been higher because the end of the delivery tube was placed to give good concentration near the face. We found it important to note at intervals whether a visible stream of mist was flowing steadily from the tube because with time the oxygen flow tends to fall and the valve may require opening a little until the mist can again be seen.

Through the kindness of its Director we had opportunity to examine nine patients in the Children's Department. Each remained under the above conditions in a tent for periods up to three hours. None showed any sign of distress. Two slept, five played with toys or books, and two, both of rather nervous type, cried a little at first but nothing more. Two of these children were suffering from bronchitis but the others were, as regards serious respiratory tract infection, virtually normal, having only slight colds. No therapeutic deductions are therefore attempted from this small group. The results of their examination are put forward simply as illustrating the degree of penicillin absorption obtainable by the method. In view of this survey treatment of a series of children suffering from really active infection has been undertaken in the Department. The early results have been decidedly encouraging and we are therefore prompted to give this preliminary description not only of the technique but of the experimental results in general because they have, we think, a significant bearing upon the whole rationale of the administration of penicillin by inhalation.

Each of these children emptied its bladder immediately before going into the tent. For examination they were removed and the skin surfaces of the genital areas and arms washed to avoid all traces of penicillin. Specimens of urine and venous blood were then collected, and also some respiratory tract cultures. These were all immediately taken to the laboratory for examination.

Of the urines the specific gravity and the reaction were first noted and the latter then brought to neutrality. After high-speed centrifuging to remove practically all debris and bacteria, the penicillin content of the supernatant urine was estimated in the usual way by setting up serial dilutions in parallel with a known saline solution, using the Oxford H strain of Staphylococcus aureus as the test organism.

The sera were examined according to the method modified from that of Fleming (1943) and recently advocated by Lourie, Collier, Ross, Robinson and Nelson (1945). Here also a series of dilutions is run parallel with those of a known saline solution. These observers found that by their method the minimal fully bacteriostatic concentration of penicillin in serum was about 0·07 units per ml. Our results are summarized in table 1.

TABLE 1

Patient	Serum Units penicillin per ml. after hours: 1	2	3	Urine Units penicillin per ml. after hours: 1	2	3
1 Girl aet. 5 yr.	0·015	0·03	0·02	0·6		1·0
2 Girl aet. 10 yr.		0·02		1·0	1·0	
3 Girl aet. 7 yr.	0·02	0·03		1·3		
4 Girl aer. 8 yr.	0·02			1·5		
5 Girl aet. 8 yr.	0·01			1·6	1·5	
6 Girl aet. 11 yr.	0·03			1·4		
7 Boy aet. 12 yr.	0·015			1·6		
8 Girl aet. 12 yr.	0·03	0·02		1·0	1·2	
9 Girl aet. 6 yr.	0·03	0·02		1·3	1·0	

As regards the penicillin content of the venous blood, these children showed relatively very low figures. In no case did they reach the minimal fully bacteriostatic level mentioned above and it is to be noted that for this level Garrod (1944) suggested an even slightly higher figure, namely, 0·1 units per ml. On the other hand these children had very large quantities in the urine. The concentration of penicillin tended to vary inversely with the specific gravity, but generally the urine carried 40 to 50 times as much as the venous blood per volume.

The relatively high urinary figure might well arise from the rapidity with which penicillin is known to be excreted. But the blood levels seemed to be very low to provoke this rate and it occurred to us that penicillin absorbed mainly into the pulmonary

circulation might show some peculiarities in its subsequent distribution.

Full-grown rabbits were therefore placed under conditions as nearly as possible the same as those encountered by the children. Instead of an actual tent a more or less cubical glass-sided cupboard (approximately 5,000 litres) was used. Ventilation, oxygen flow and aerosol dispersion were maintained as before. The animals took very little notice of the mist and showed no sign whatever of distress. They remained in the cupboard for an hour to an hour and a half. On removal they were instantaneously killed by a single blow on the back of the head and the thorax and abdomen were at once opened. By needle and syringe aspiration blood samples were at once taken from the right and left ventricles. Meanwhile an assistant had clamped off a peripheral area of the lung to arrest all circulation. Avoiding large bronchi, about 2 g. of the isolated lung tissue was cut away with scissors, quickly weighed, and ground up with sand in 10 ml. of normal saline. Filtration followed immediately and we estimated the penicillin content of the filtrate. The penicillin levels at the different sites are set out in table 2.

TABLE 2

Rabbit	Serum units per ml.		Lung
	Right ventricle	Left ventricle	Units per g.
1	0·02	0·35	3·1
2	0·01	0·25	2·0
3	0·03	0·35	0·8
4	0·015	0·20	1·2
5	0·03	0·30	3·0

It will be seen that after its absorption through the lungs there is decidedly more penicillin in the blood of the left ventricle than in that of the right. Accordingly there must be a much higher concentration passing to the tissues in the arterial blood than that indicated by the results of venepuncture estimations. The low blood figures in the children are not necessarily an index of the bacteriostasis to be expected. But a further significant result of the animal tests is the demonstration of the very considerable concentration of penicillin found in the peripheral lung. The average figures for the different sites are: Right ventricle blood 0·02 units per ml., left ventricle blood 0·29 units per ml. and lung 2·0 units per g.

Discussion

If one adds to the above evidence the fact that nose and throat swabbings and any sputum taken from the children after only a quarter-of-an-hour in the tent are loaded with penicillin and when plated and incubated will grow no penicillin-sensitive organisms, it seems clear that inhalation of the aerosol stands a good chance of influencing respiratory tract infections favourably quite apart from any effect of the penicillin circulating in the blood. That free absorption into the blood stream does occur cannot be in doubt and disappointing though the low venous blood concentrations may at first sight appear to be, the above direct animal experiments indicate that during continuous inhalation of the aerosol penicillin is reaching distant tissues in significant quantities. Therefore we feel that the method, which is quite simple in operation, causes no undue nursing complications and is perfectly well tolerated by patients, deserves careful clinical trial.

Summary

A method is described by which continuous inhalation of penicillin aerosol can be combined with the treatment in oxygen tents of children suffering from acute respiratory tract infections.

As a result of examining specimens from children in such tents and of direct animal experiment, figures are given for the blood, urinary and pulmonary penicillin concentrations which may be obtained by the method.

There is relatively high concentration in the lung and in the arterial blood during continuous inhalation.

We wish to express our sincere thanks to Dr. R. W. B. Ellis for placing the facilities of his Department so freely at our disposal. For the penicillin used we are greatly indebted to the Penicillin Clinical Trials Committee of the Medical Research Council. In the wards the assistance of Miss Duncombe, Sister in charge, has been invaluable, and to Mr. W. H. Clark, F.I.M.L.T., and Mr. A. C. Lock, M.I.E.E., we are most thankful for unfailing technical advice. The generator and the drawing for fig. 1 were made by Aerosols Ltd., 10, Portman Street, W.1.

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PENICILLIN IN THE TREATMENT OF NEONATAL SEPSIS

BY

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The object of this research has been to determine the place of penicillin in the treatment of neonatal sepsis. It is well known that in the neonatal period only a minority of cases present symptoms which enable an exact diagnosis to be made either of the site, or sites, of infection or of the nature of the infecting agent. Many of these patients present a distinctive clinical picture, however, and have an illness of sudden onset with some or all of the following symptoms: fretfulness or apathy, refusal to feed, diarrhoea, vomiting, and an abnormal fall of the post-natal birth weight, or a downward deflection of the weight curve if this has begun to climb. The temperature may be raised at some period of the illness, but absence of fever will not exclude the presence of infection. The respiration rate may be increased and icterus may seem more pronounced than would be expected in physiological jaundice of the newborn. The condition sometimes assumes epidemic proportions in maternity hospitals. When diarrhoea predominates there is then a tendency to label it epidemic diarrhoea of the newborn and to regard it, sometimes with little further investigation, as a primary gastro-enteritis of unknown etiology.

Careful and detailed autopsies on cases of neonatal sepsis, especially when dehydration has been in some measure controlled, will very rarely show any lesions in the intestinal tract, but will often show evidence of infection elsewhere, especially in the respiratory tract. Histological examination will frequently reveal acute inflammatory reaction in the nose, larynx and pharynx, lungs and nearly always in the middle ears. Some cases may show only thrombi in intracranial or renal veins, and it is then impossible either to implicate or to exclude a low-grade and disseminated bacterial infection. It is not useful at the moment to discuss whether symptoms, which in many of these cases might suggest a primary gastro-enteritis, result from a primary invasion by viruses, bacteria or both pathogenic agents in symbiosis through the respiratory tract or other portal of entry. It is enough to emphasize that, if dehydration is controlled, bacterial infection, especially of the respiratory tract, be it primary or secondary, plays a very important rôle and often determines the fatal outcome.

While the effect of penicillin must also be assessed in cases where the diagnosis can be more fully established, the main object of the present investigation has been to study its influence on the above type of case on an admittedly empirical basis. The cases treated may have been produced by different viruses and bacteria and their evolution was probably influenced by secondary microbic invasion. Such secondary infection may result from cross-infection from other infants, or from mothers or attendants, in spite of the segregation of infants in small nurseries and a careful nursing technique; it may also be due to organisms which are normally saprophytic on the skin or epithelial-lined passages of the infant. A careful and detailed clinical and autopsy study may indicate something of the various factors contributing to death, but there is no hope at present of making any scientifically satisfactory, or even clinically useful, subdivision of the majority of these cases.

Selection of Clinical Material

Eighty-nine cases, all within the first month of life, have been included in this survey. Eighteen cases were treated with penicillin, chiefly during the early part of the study, on an individualized basis and without collateral controls, and these will only be referred to later. The other seventy-one cases were treated on a definite plan and thirty-five received penicillin and sulphadiazine and thirty-six sulphadiazine only. Infants in the neonatal department of the Jubilee Maternity Department of the Belfast City Hospital were kept under specially close supervision. Any refusal to feed, the onset of diarrhoea or vomiting, abnormal loss of weight, rise of temperature, increase in respiration rate, or any sign of toxicity was at once investigated and the infant transferred to a sick nursery under a staff specially trained and instructed in the procedures of this investigation. A detailed physical examination was made, but blood cultures or catheter specimens of urine were not examined in this series. In the initial stages blood cultures are unlikely to be helpful because even three or more cultures are often negative and the significance of many of the

organisms recovered may be questioned even when the most careful technique is employed. Treatment cannot be withheld until repeated cultures have been taken. The decision as to whether the baby was infected or not was therefore made on the clinical evidence alone. Alternative cases of sepsis were assigned either to receive sulphadiazine therapy in the control group or to receive, in addition, penicillin therapy in the test group. Cases were treated until they recovered or died.

Three cases receiving penicillin and one receiving sulphadiazine only died within twenty-four hours, and one test and two control cases were taken home against advice while the outcome was still in doubt. One case in each group was shown at autopsy to have thrombotic lesions much older than the period of chemotherapy, and one control case was found at autopsy to have a developmental defect (case 2; Morison, 1945). It has been thought right to exclude these five test group and five control group cases. In this series there are therefore sixty-one cases available for analysis. Owing to the number and severity of the cases encountered the hospital was at one period closed and thoroughly cleansed and disinfected. It was a definite clinical impression that the nineteen cases treated after this showed, when they were compared with the first forty-two cases treated, less marked intestinal symptoms and more obvious involvement of the respiratory system. It has been thought useful to distinguish these two groups and to give the results from each separately, followed by the total (e.g. 9+5=14).

The birth weights and the weights at onset of illness show a rather wide range of values. In Table 1 the means of these values are given after the cases have been divided according to treatment and outcome. The mean ages at onset are also given, but here an accumulation of values a little below the mean and a few far above it made the calculation of figures for the standard deviations of no consequence. On analysis, however, the groups were very similar in age composition. The mean weight is lowest in the group dying after treatment with penicillin and sulphadiazine. This is not statistically significant and it was due to an unfortunate, but entirely unintentional, inclusion of all six infants of less than 5½ lb. in the test group. Four of these premature infants died. It has been thought necessary, therefore, to give additional figures to show the effect of exclusion of all these premature infants.

Therapeutic Procedures

It was not thought justifiable to withhold from either group the possible benefit of sulphadiazine, especially in view of the frequency of intestinal symptoms. Sulphadiazine has been found valuable not only in combating possible enteral pathogens, but also for its action on parenteral infections, the toxins of which are probably very often responsible for diarrhoea. The control group, therefore, received 0·25 gm. of sulphadiazine every three hours and the test group in addition had 1500 units of penicillin in ½ c.c. sterile distilled water given by intramuscular injection with a fine needle every three hours. This represented in nearly every case well over 1500 units per pound of body weight per twenty-four hours and, judged on this basis, on the reports of other workers and on a few observations made here, should have produced very satisfactory bacteriostatic levels. Control of dehydration and feeding was similar in both groups. Oral thrush infection was controlled by 2 per cent. aqueous solution of gentian violet.

Results

Control Series. The results are presented in Table 2. It will be seen that fourteen controls (sulphadiazine treated) lived and seventeen died, and that thirteen treated (sulphadiazine and penicillin treated) cases lived and seventeen died. If premature infants are excluded there are still fourteen controls who lived and seventeen who died, while eleven treated cases lived and thirteen died. It is evident, even without statistical analysis, that these figures hold out no hope of demonstrating any difference, if such exists, between the two groups with a number of cases which there is any immediate likelihood of obtaining, even by a large-scale investigation.

When recovery or death occurred within two or three days it may be suggested that the whole infection was due to a virus, and that only when the illness was prolonged beyond this period could penicillin exert an influence on the secondary bacterial flora. The data given in Table 2 allows the exclusion of cases whose outcome was determined by the second or third day. Even after this very questionable procedure the results, admittedly on undesirably smaller groups, provide no evidence which, on statistical analysis, favours penicillin therapy.

Further information might be obtained by a study of the duration and severity of illness in the two groups. In all but nine cases daily observations of the body weight were made. In cases which recovered, the number of days of illness before the downward movement of the weight curve was reversed probably measures the duration of the illness as well as any subjective clinical impression.

TABLE 1

MEAN WEIGHT AND AGE OF INFANTS IN THE VARIOUS TREATMENT GROUPS

	Sulphadiazine		Penicillin + Sulphadiazine			
			All cases		Prematures excluded	
	Lived	Died	Lived	Died	Lived	Died
Birth weight (lb.)	7·38±1·06	7·51±0·84	7·40±1·07	6·38±1·38	7·93±0·98	7·17±0·80
Onset weight (lb.)	6·56±0·97	6·63±0·87	6·78±1·66	5·71±1·31	7·55±1·23	6·34±0·78
Mean age at onset (days) ..	6·1	4·9	7·7	6·0	8·0	5·0

TABLE 2

NUMBER OF PATIENTS RECOVERING AND DYING AND DURATION OF ILLNESS AND LOSS OF WEIGHT

	Sulphadiazine alone (No prematures)	Penicillin + sulphadiazine	
		All cases	Prematures excluded
RECOVERY			
Total	9 + 5 = 14	8 + 5 = 13	8 + 3 = 11
Weight fall reversed within:			
2 days	5 + 1 = 6	2 + 4 = 6	2 + 3 = 5
3 days	7 + 2 = 9	4 + 4 = 8	4 + 3 = 7
4 days	9 + 5 = 14	5 + 4 = 9	5 + 3 = 8
Weight loss under:			
4 oz.	4 + 3 = 7	4 + 4 = 8	4 + 3 = 7
8 oz.	8 + 5 = 13	6 + 5 = 11	6 + 3 = 9
over 8 oz.	1	2	2
DEATH			
Total	13 + 4 = 17	12 + 5 = 17	9 + 4 = 13
Death within:			
2 days	0 + 1 = 1	6 + 1 = 7	4 + 0 = 4
3 days	4 + 2 = 6	7 + 3 = 10	5 + 2 = 7
4 days	9 + 4 = 13	9 + 3 = 12	7 + 2 = 9
5 days	11 + 4 = 15	10 + 3 = 13	8 + 2 = 10
after 5 days	2	2 + 2 = 4	1 + 2 = 3
Total weight loss:			
under 4 oz.	1	3	2
8 oz.	3	8	5
12 oz.	8	11	8
16 oz.	10	11	8
over 16 oz.	3	1	1

The actual loss of weight is probably less useful as many cases became ill during the period of physiological weight loss. In cases which died a prolongation of the period of illness or a reduction of the weight loss might suggest some benefit. The wide scatter of these values and the small numbers in each class have made statistical analysis impossible. This data has, however, been tabulated in Table 2. Treated and control cases show no constant or significant difference and there is no indication that penicillin has been of any benefit.

Individualized therapy. Four cases treated in the Jubilee Maternity Hospital yielded little information and neither penicillin nor sulphadiazine, singly or together, appeared to influence somewhat protracted, but low-grade, sepsis. Fourteen cases were treated in the Royal Maternity Hospital. In six the outcome was highly satisfactory but, in review, the indications for therapy were scarcely sufficient to justify a claim that neonatal sepsis was certainly present. Two cases died despite adequate amounts of penicillin. One of these was a 28-week premature infant of 2 lb. 11 oz., and here 10,000 units daily from the nineteenth to the twenty-fifth day of life failed to control a peritonitis from which only enterococci and B. coli were isolated and which was secondary to an infected umbilicus. In the other case a full-time infant died on the twelfth day from pneumonia after six days' treatment with 8000 units daily and then two days on 16,000 units daily. The premature infant received only a short preliminary course of sulphadiazine, but in the second case sulphadiazine was given throughout.

Four cases which did not respond initially to sulphadiazine are of interest, and penicillin probably contributed to the favourable outcome. One was a 32-week premature infant of 2 lb. 14 oz. whose blood culture on the eighth day of life, and while he was receiving sulphadiazine, gave a pure growth of Staphylococcus aureus. He was given 18,125 units in the next twenty-four hours, and the blood then gave complete stasis by Fleming's method in a dilution of 1 : 64. A further course of 13,125 units was given over three days, but he appeared entirely cured. A troublesome case of pemphigus reacted very favourably to 21,500 units given over four days. The other two cases appeared clinically to be cases of pneumonia and responded well to 1000 units three-hourly, and therapy was stopped after the fourth and fifth days.

Two cases received penicillin and sulphadiazine at the same time. One was probably a primary pneumonia. The other received 8000 units daily from the sixteenth day of life when he was fretful, appeared dehydrated and had a distended, tender abdomen, but an apparently healed umbilicus. From the twenty-fifth day of life there was an abundant discharge of pus from below the umbilicus and this contained Staphylococcus aureus. Penicillin was continued until the thirty-fifth day and contributed to the favourable outcome in this case of umbilical infection.

In this group the cases which responded to penicillin resembled somewhat those infections of later childhood or adult life which are amenable to penicillin. There was some evidence of a primary infection, presumably by an organism susceptible to penicillin, and apparently the condition of the infant, or the location of the lesion, did not favour heavy secondary infection, especially of the respiratory tract by resistant organisms.

Discussion of Results

It will be appreciated that this survey is a comparison of combined penicillin and sulphadiazine

treatment with sulphadiazine therapy alone. At one time neonatal infections may be mild and the death rate low and at another the mortality may be high. It is, therefore, impossible to compare results from year to year. There is a clinical impression that sulphadiazine does make some contribution to the control of neonatal infections. In certain well-defined conditions such as staphylococcal infections, and probably in some cases of primary bacterial pneumonia penicillin possesses some advantage over sulphadiazine. It would seem, however, that the organisms responsible for much of the sepsis in the newborn are no more susceptible to penicillin than to sulphadiazine. It may be suggested that death is, therefore, due to a septicaemia or toxaemia originating from the bowel, where the epithelial barrier may be damaged. The severity of the intestinal disturbance is, however, little guide to the outcome, and death often occurs when the intestinal symptoms have abated. In the absence of anatomical lesions in the bowel wall, of reaction in the mesenteric lymph glands or of pathogenic intestinal bacteria, and in cases under oral treatment with a sulphonamide derivative, it would be well to look elsewhere before accepting this superficially attractive hypothesis.

The high incidence of respiratory tract infections has already been commented upon. It would be reasonable to hope, if the bacteria concerned were pathogens derived from the respiratory tract of adults, that a high proportion would be sensitive to penicillin. It is possible, however, that the organisms are derived from the normal flora of the nose and throat of the newborn, and that toxins acting on immature structures, associated virus infection or some other factors, depress the normal defence mechanisms which include the protective reflexes guarding the respiratory tract. Torrey and Reese (1944, 1945) have reviewed the somewhat conflicting reports on the initial aerobic flora of the newborn. They confirm the observation of Kneeland (1930) that many potential pathogens of the adult respiratory tract show little tendency to persist or grow out in the nasopharynx of the newborn infant. But, since Staphylococcus aureus was present in almost 90 per cent. of sixty-three infants by the end of the first week, it is unlikely to be absent from lesions caused by any extension of organisms from the nose or throat. Though Kneeland and Torrey and Reese have reported a lower incidence of adaptation of coliform organisms to the upper respiratory tract, the incidence has been high in other series (Witkowski, 1935). These and other penicillin-resistant organisms are probably nearly always present and capable of contributing to the production of fatal lesions. It is not possible to say if penicillin has only eliminated penicillin-sensitive organisms to allow penicillin-resistant organisms to produce very similar lesions. In 1939 MacGregor emphasized the high incidence of B. coli infections in neonatal pneumonia. While coliform organisms are only too easily isolated from the dead newborn infant it must be admitted that this organism, even in non-treated cases, often appears to be the only bacterial pathogen at the time of death. Occasionally in previous cases of this kind we have separated a few colonies of Staphylococcus aureus from a heavy growth of coliform organisms. In the present series the autopsy material was rarely fresh enough to permit satisfactory bacteriology, but no penicillin-sensitive organisms were recovered. In many cases of this kind in the newborn it is probable that the type of bacteria causing the pneumonia is less important than the conditions rendering the respiratory tract of the newborn abnormally susceptible to bacterial infection.

It should be emphasized that there is no panacea for neonatal sepsis. While penicillin may be highly beneficial in a few cases, where a penicillin-sensitive organism can be solely incriminated, its widespread exhibition can only distract attention from such symptomatic treatment as the control of dehydration and the prevention of aspiration pneumonia by good nursing. Very extensive researches, and perhaps radical changes in our conceptions of the interaction of infecting agents with one another and with epithelial surfaces, must precede advances in the treatment of neonatal sepsis. Since chemotherapy cannot control or cure the more widespread and more infectious forms of neonatal sepsis, the proper policy is to emphasize the necessity for its prevention by continued improvement in the provision of adequate accommodation, facilities for segregation and rigid nursing technique.

Summary

A diagnosis of neonatal sepsis was made in seventy-one cases and every alternative case was treated with both penicillin and sulphadiazine. The remaining cases received sulphadiazine alone and served as controls. A study of the sixty-one cases which were suitable for analysis failed to show that penicillin increased the recovery rate, or influenced either the duration of the illness or the severity of decline in body weight. The importance in this connection of bacterial infection, especially of the respiratory tract by a potentially variable flora, is discussed. A few cases, chiefly of Staphylococcal infection, were thought to benefit in a further group of eighteen cases treated without controls.

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THE SULPHONAMIDES IN THE TREATMENT OF INFECTIONS IN INFANCY

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Although there is now a considerable literature dealing with the use of sulphonamides in many diseases, there are few articles on their use in infancy. Some authors, e.g. Leathart (1943), Field et al. (1943), Patterson and Stewart Smith (1944), mention, sometimes in a rather unenthusiastic manner, that sulphonamides were given but supply no details. The material of present study consists of 415 infants under the age of ten months who suffered from some infection and were, for the most part, treated with one of the sulphonamide group of drugs. An attempt has been made to assess the value of these drugs in such infections. Meningococcal meningitis and gonorrhoeal ophthalmia have not been included. The cases were treated in Alder Hey Childrens' Hospital, Liverpool, which deals with approximately 1000 infants per annum and in Walton Hospital, Liverpool, which has a large maternity department. The latter department dealt with 3700 confinements in 1943 and one part of this investigation was made possible by the unfortunate occurrence of an outbreak of neonatal gastroenteritis.

Scheme of treatment. In order to standardize treatment in the two hospitals it was decided to employ the following doses by mouth: for mature infants, an initial dose of 0·75 gm. to 1·0 gm., followed by 0·5 gm. four-hourly; and for premature infants an initial dose of 0·5 gm. followed by 0·25 gm. three-hourly. This is the system of dosage advocated by Henderson (1943) for sulphaguanidine. Glucose-saline was given in the early stages of the illness to assist in the elimination of the drug and to overcome dehydration if present. In more severely dehydrated infants continuous intravenous drip salines were administered as required. It was also decided to use the drugs as far as possible according to the following system:

A. Neonates—up to one month. (a) Premature. (b) Mature.

B. Infants—from one to nine months.

These groups were then subdivided as follows:

(1) ENTERAL INFECTIONS, i.e. where no evidence of parenteral infection could be found :

(a) Neonatal gastroenteritis	Sulphaguanidine. Sulphasuxidine.
(b) Gastroenteritis in older infants	No chemotherapy.
(2) PARENTERAL INFECTIONS.	
(a) Bronchopneumonia Pneumonia.	Sulphapyridine. Sulphathiazole. Sulphadiazine. Sulphamezathine.
(b) Nasopharyngitis. Bronchitis.	Sulphapyridine. Sulphathiazole. Sulphadiazine. Sulphamezathine.
(c) Otitis media. Mastoiditis.	Sulphapyridine. Sulphathiazole. Sulphadiazine. Sulphamezathine.
(d) Pyelitis.	Sulphapyridine. Sulphathiazole. Sulphadiazine. Sulphamezathine.
(e) Skin sepsis.	Sulphathiazole. Sulphadiazine. Sulphonamide cream.

Classification of results. The classification of the results of an investigation such as this is a difficult problem. Three methods suggest themselves.

(1) BACTERIOLOGICAL. Bacteriological classification would obviously be the most satisfactory method. Unfortunately bacteriology in infantile infections is inconclusive and therefore does not commend itself as a basis of classification. For example, the bacteriology of the faeces in cases coming under the title of ' gastroenteritis ' is highly unsatisfactory; swabs from discharging ears almost invariably give a mixed growth; specimens of urine are often difficult to obtain and in pneumonia bacteriological investigations are not practicable.

(2) CLINICAL. Classification according to disease is a suitable method as far as it goes. Unfortunately its success depends upon individual interpretation of clinical signs, which is notoriously difficult in infancy. Certain infections are much less common than others and even when cases are grouped together the numbers are too small to be of statistical significance.

(3) ACCORDING TO THE DRUG USED. This method is also unsatisfactory because the sulphonamides have no clearly defined specificity and equal results may be obtained in the same type of infection with different drugs.

The bacteriological method of classification being out of the question, the present series has been subdivided on a plan which includes the second and third methods, i.e. by a classification based on the clinical findings and the sulphonamide drug used.

Part I

(1) Enteral infections

(a) **Neonatal gastroenteritis.** All the cases in this group fell within the neonatal period and consisted of babies showing signs of gastroenteritis for which no parenteral cause could be found on careful clinical examination. Two sulphonamide drugs were used, sulphaguanidine and sulphasuxidine, and a small group were treated without sulphonamide. There are 128 cases in the whole group, 57 treated with sulphaguanidine, 52 treated with sulphasuxidine and 19 had no sulphonamide.

SULPHAGUANIDINE

GENERAL FIGURES. Of the 57 cases, ten died (17·5 per cent.). There were 34 males and 23 females. Using the standard of 5½ lb. birth weight, there were nine premature infants and 48 mature infants. Of the nine premature infants four died (44·4 per cent.) and six (12·5 per cent.) of the mature infants died. Two cases had two attacks and one of them died at the age of four months.

SYMPTOMS. Date of onset. The disease began between four and 24 days after birth (average 10·7 days).

Diarrhoea. Every case had diarrhoea and in twelve the diarrhoea was severe.

Vomiting. The majority had vomiting, but in seventeen there was no vomiting.

Dehydration. In eighteen there was no dehydration, thirty had mild dehydration and nine were considerably dehydrated.

Pyrexia. Thirty were apyrexial throughout and 27 were pyrexial in varying degree. The temperature varied from 99° F to 104·8° F.

Weight loss. Every case suffered some weight loss. This varied from 3 to 26 oz. (average 10 oz.).

GENERAL ASSESSMENT. Severe, 13 (death rate 61·5 per cent.); moderate, 16; mild, 28.

Among the mild cases two died, one some months later and the other, a premature infant, died eleven days after recovering from the gastroenteritis. These two cases might reasonably be deducted from the deaths and in that case the death rate would be 14 per cent. None of the moderate group died and the remainder of the deaths were severe examples.

PROGRESS OF THE DISEASE. Duration of pyrexia. Eighteen cases were pyrexial for only one day after the drug was begun, although some had been pyrexial for four to seven days previously. In two of the deaths the temperature was uncontrolled. Five patients who died were apyrexial throughout and two were apyrexial in one day.

Stools. In those who recovered stools became normal in one to ten days (average 3·2 days).

Weight. Weight lost as a result of the illness was regained in 36 cases in periods varying from three to twenty-four days (average 12·9 days). Eleven patients were removed from hospital against advice and their subsequent history is not known.

BACTERIOLOGY. Faeces were examined in fifteen cases, with negative result in eleven cases. In four cases B. Morgan I, usually regarded as non-pathogenic, was grown.

DOSE OF THE DRUG. Those of the mature infants who recovered received doses ranging from 3·75 gm. to 27·25 gm. (average 12·8 gm.). In the case of premature infants the total dose varied from 1·25 gm. to 8·25 gm. (average 4·8 gm.).

COMPLICATIONS OF THE DRUG. One patient developed a macular rash and three developed oedema of legs and lower abdomen. These three cases had respectively a total dose of 14·25 gm., 12 gm. and 16·25 gm. of the drug. Two were unfortunately taken from hospital against advice and their ultimate fate is unknown. The third case died and the suspicion that the oedema might be due to renal damage was not confirmed at post-mortem examination.

COMPLICATIONS OF THE ILLNESS. One had continued pyrexia and developed signs of bronchitis, but ultimately recovered. In another the left ear began to discharge five days after the onset of the diarrhoea which was almost certainly parenteral in origin. Another developed right acute otitis media some weeks afterwards and ultimately died. Three had conjunctivitis and one mild jaundice. One had a congenital haemangioma of the left arm and wrist drop.

POST-MORTEM FINDINGS. Two of the deaths took place three months and eleven days respectively after recovery from the attack of enteritis. In the first of these bronchopneumonia and right acute otitis media were found at post-mortem examination ; and in the second, which was 3 lb. 10 oz. at birth, no cause other than prematurity was found. In a third case permission for examination was refused. Of the seven remaining cases five had bronchopneumonia, accompanied in one case by bilateral acute otitis media which did not seem to be a secondary occurrence. The sixth case was a premature infant of 4 lb. 1 oz. at birth, which was found to have right acute otitis media. The seventh case was the one which became oedematous. This infant had been very ill from the outset and was found to have right acute otitis media, left empyema, and pus in the right sternoclavicular joint, the organism being a staphylococcus. Section of the kidney showed no evidence of blockage by crystalline deposits of the sulphonamide.

SULPHASUXIDINE

GENERAL FIGURES. Of the 52 cases, eleven died (21·1 per cent.). There were 28 males and 24 females; ten were premature infants and 42 mature infants. Of the ten premature infants six died (60 per cent.) and five (11·9 per cent.) of the mature infants died. Two patients had two attacks.

SYMPTOMS. Date of onset. All fell within the neonatal period and the disease began between four to twenty-eight days after birth (average 11·9 days).

Diarrhoea. With one exception every case had diarrhoea and in two it was severe.

Vomiting. In 26 cases there was no vomiting.

Dehydration. In 21 cases there was no dehydration, while 26 had mild dehydration and five severe dehydration.

Pyrexia. Twenty-six were apyrexial and 26 were pyrexial in varying degree, the temperature varying at its maximum from 99°F. to 105·4° F.

Weight loss. With the exception of two cases in whom weight remained stationary, every case lost some weight, varying from 4 to 24 oz. (average 10 oz.).

GENERAL ASSESSMENT. Severe, 15 (death rate 66·6 per cent.); moderate, 18; mild, 19.

Among the mild cases there were no deaths. One death occurred in the moderate group, a premature infant which developed cyanotic attacks due to bronchopneumonia a fortnight later. If this death is not included, the mortality rate falls to 19·2 per cent. The remainder of the deaths were severe cases.

PROGRESS OF THE DISEASE. Duration of pyrexia. Twenty infants were pyrexial for only one day after giving the drug. One infant was pyrexial for twelve days and one infant who died was uncontrolled. Seven of those who died were apyrexial throughout. Of the remaining fatal illnesses, two were pyrexial for one day and one for three days.

Stools. Stools became normal in those who recovered in one to seven days (average 3·3 days).

Weight. Weight lost as a result of the illness was regained in 36 cases in periods varying from four to thirty days (average 14·3 days). In four cases the after-history is not known as they were taken from hospital against advice.

BACTERIOLOGY. Stools were examined in 31 cases, with negative result in 27. Four grew B. Morgan I. Three were examined twice with negative result and in three the urine was also negative.

DOSE OF THE DRUG. Of the mature infants who recovered and had a full course, the total dose varied from 6·25 gm. to 20·75 gm. (average 12·6 gm.). In the case of premature infants the total dose varied from 6·5 gm. to 10·75 gm. (average 9·3 gm.).

COMPLICATIONS OF THE DRUG. One case developed haematuria and the drug was instantly stopped. Kapilon was given and no further trouble ensued. Another developed slight oedema of the legs which resolved satisfactorily.

COMPLICATIONS OF THE ILLNESS. In three cases, soon after the onset of the enteritis, symptoms of parenteral infection which was the probable cause of the illness, became apparent: one, pneumonia; one, nasopharyngitis; and one, otitis media and bronchitis. One had had bronchitis ten days previously. As already mentioned, one premature infant had a cyanotic attack in which it died. Three were jaundiced and one was a case of erythroblastosis foetalis. Six developed mild thrush and one had congenital heart disease.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in eight cases. The premature infant with the cyanotic attack had bronchopneumonia. In the seven remaining cases all save one showed evidence of parenteral infection as follows: two with bronchitis and otitis media, two with bronchitis alone, one with bronchitis and prematurity and one with bronchopneumonia and otitis media.

NO CHEMOTHERAPY

GENERAL FIGURES. Of the nineteen cases, five died (26·3 per cent.). There were eleven males and eight females, among whom were nine premature infants and ten mature infants. Of the nine premature infants, four died (44·4 per cent.) and one of the mature infants died (10 per cent.).

SYMPTOMS. Date of onset. All began within the neonatal period between 6 to 28 days after birth (average 13·4 days).

Diarrhoea. All but three had diarrhoea. Two of those without diarrhoea died.

Vomiting. Eight cases had vomiting, one severely.

Dehydration. Ten were dehydrated but none severely.

Pyrexia. Ten cases were apyrexial and seven were pyrexial, temperature varying from 99·2 F. to 101·6° F. In two cases there is unfortunately no record.

Weight. Sixteen cases lost weight in amounts varying from 5 to 24 oz. (average 10·9 oz.). In three cases weight remained stationary.

GENERAL ASSESSMENT. Severe, 6 (death rate 83·3 per cent.); moderate, 5; mild, 8.

There were no deaths in the mild or moderate groups.

PROGRESS OF THE DISEASE. Duration of pyrexia. Four cases were pyrexial for one day after commencing treatment, three were pyrexial for two to ten days and ten were apyrexial throughout. Three of the infants who died did not have pyrexia and one was pyrexial for five days. In one fatal case the temperature is not known.

Stools. The stools became normal in those who recovered in two to seven days (average 3·4 days).

Weight. Weight lost as a result of the illness was regained in seven cases in periods varying from 8 to 19 days (average 11·7 days). Seven cases were removed from hospital against advice.

COMPLICATIONS OF THE ILLNESS. Five had mild thrush, three were jaundiced and two were thought to have developed bronchopneumonia.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in four of the five fatal cases. The results are as follows: one, bronchitis; one, bronchopneumonia and bilateral acute otitis media; one, bilateral acute otitis media. In the fourth case prematurity was the only cause of death found.

Comment

TABLE I

	Sulphaguanidine 57 cases		Sulphasuxidine 52 cases		No chemotherapy 19 cases	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Premature	9	15·7	10	19·2	9	47·3
Mature ..	48	84·3	42	80·8	10	52·7
Mild ..	28	49·1	19	36·5	8	42·1
Moderate..	16	28·0	18	34·6	5	26·3
Severe ..	13	22·8	15	28·8	6	31·3
Deaths ..	10	17·5	11	21·1	5	26·3

It will be seen from the comparative table (table I) that of the first two groups the sulphasuxidine group is probably the more severe. The group with no chemotherapy is the most severe owing to the high proportion of premature infants and this group has

the highest death rate. The relatively small difference in the mortality rates between the drug-treated and the non-drug-treated groups should be noted.

The rationale of using these sulphonamide drugs lies in the fact that they are poorly absorbed from the intestinal tract. Approximately two-thirds of sulphaguanidine are absorbed while one-third is excreted in the faeces in high concentration. Only 5 per cent. of sulphasuxidine is absorbed (M.R.C. War Memorandum No. 10). Drugs acting in this way might be expected to operate against an infection of the gastrointestinal tract and of the two sulphasuxidine should be the better. Other workers have found that these drugs exert a good effect in the dysentery group of diseases but in neonatal gastroenteritis no satisfactory bacteriological explanation in the faeces has been forthcoming. The results in the sulphasuxidine group are not materially better than those in the sulphaguanidine group. The post-mortem findings in the present series show the presence of parenteral infection in the great majority of cases; such infection is not likely to be benefited by the usual mode of action of these sulphonamides, though possibly the portion of the drug absorbed is responsible to some extent for the recoveries. The parenteral infections found are in no way different from those often found in older infants suffering from gastroenteritis and the belief is growing that there is no essential difference between the so-called neonatal gastroenteritis and the gastroenteritis of older infants. This view has recently been expressed by Burns and Gunn (1944). On the other hand, MacGregor (1939), describing her experience of neonatal pneumonia, found that in the neonatal period organisms of the colon bacillus group and staphylococcus aureus were the commonest responsible pathogens. She also states that coliform infections are confined to the neonatal period. It is possible then that drugs such as sulphaguanidine and sulphasuxidine which reduce the number of enteral coliform organisms, may also exert an effect in parenteral infections of the type found at post-mortem examination in the present series.

Some of the recorded figures are interesting. The death rate in an outbreak described by Craig (1936) was 26·8 per cent. In three outbreaks described by Ormiston (1941) the following were the figures.

	Total death rate per cent.	Death rate in serious cases per cent.
Outbreak A ..	18·5	62
Outbreak B ..	30·1	81
Outbreak C ..	38·0	—

In outbreak C sulphathiazole and sulphapyridine were tried without benefit. In the present series the total death rates in the three groups are 14, 19·2 and 26·3 per cent. respectively while among the severe cases the corresponding figures are 61·5, 66·6 and 83·3 per cent. If these figures are compared it will be seen that in the drug-treated groups the total death rates are slightly lower than in Ormiston's series but in the severe cases the death rates are uninfluenced. Henderson (1943) gives his figures before and after the use of sulphaguanidine. Before sulphaguanidine the death rate varied from 14 to 31 per cent. and after, it was 10 per cent. and he speaks very highly of this treatment. Collis (1943) reports cure in two-thirds of cases by the use of sulphaguanidine whereas McSweeney (1942) reports no material benefit. The latter states that 50 per cent. of those treated with sulphaguanidine died and 38·2 per cent. of those not so treated died. There are few references to the use of sulphasuxidine. Twyman and Horton (1943) report favourable results. Of 22 cases of neonatal diarrhoea, eleven were treated with sulphasuxidine with two deaths, due in their opinion to inadequate dosage, whilst there were four deaths in the control group and 'weight gains for eight days of infants treated with succinyl-sulphathiazole were not matched in seventeen days by the untreated infants.' They recommend the administration of vitamin K to infants treated with this drug because the reduction of the coliform organisms caused by the drug inhibits the absorption of the vitamin and promotes bleeding tendencies. Certainly the baby in the present series who developed haematuria seemed to benefit by the use of vitamin K. In Gunn's (1943) 22 severely dehydrated cases, the case fatality was 45·5 per cent. and he reports little effect from the drug. He also reports no benefit from sulphaguanidine. Lewes (1943) reports a case, ultimately found to have bilateral mastoiditis, in which two courses of sulphasuxidine had no effect.

The views on this matter are therefore conflicting, possibly due to some epidemiological difference in the outbreaks described. From the present series it would seem that the total death rate can be reduced to some extent but the treatment must be begun as soon as possible since in severely affected infants these drugs appear to exert little benefit.

(1) Enteral infections

(b) **Gastroenteritis in older infants.** In this group there are 24 cases and again the drugs employed are sulphaguanidine and sulphasuxidine. The group also contains a number who had no chemotherapy. The group displayed the following symptoms:—24 had diarrhoea, 22 vomiting and 21 dehydration. Thirteen were pyrexial and eleven were apyrexial throughout. Loss of weight occurred in every case.

Sulphaguanidine

General figures. There were eight cases, five males and three females of whom two were premature infants. No deaths occurred.

General assessment. Severe, 7; mild, 1.

Progress of the disease. Duration of pyrexia. In four cases temperature lasted for 24 hours and in two cases for two days. The remainder were apyrexial throughout.

Stools. The stools became normal in two to nine days (average 5 days).

Dehydration. This was severe in six cases and four required intravenous fluids.

Weight. All gained weight except one which was taken from hospital against advice.

Bacteriology. Faeces were examined in five cases with negative results.

Total dose of the drug. For the mature infants the average total dose was 19 gm. and for the premature infants 8·25 gm. No complications of the drug were observed.

Complications of the illness. One case had

congenital heart disease and congenital corneal opacities.

Sulphasuxidine

General figures. There were seven cases, three males and four females. All were mature infants and no deaths occurred.

General assessment. Severe, 1; moderate, 3; mild, 3.

Progress of the disease. Duration of pyrexia. Three were pyrexial for one, two and four days respectively. The remainder were apyrexial throughout.

Stools. The stools became normal in one to seventeen days (average 4·5 days).

Dehydration. Only in one case was dehydration sufficiently severe to necessitate intravenous fluids.

Weight. All made satisfactory gain in weight.

Bacteriology Faeces were examined in six cases with negative result.

Total dose of the drug. The average total dose of the drug was 16 gm. and no complications were observed.

Complications of the illness. One case developed right acute otitis media about the sixteenth day in hospital which responded to sulphathiazole, and glycerin and carbolic acid drops.

No Chemotherapy

General figures. There were nine cases, four males and five females, among whom was one premature infant. One death occurred.

General assessment. Severe, 5 with 1 death; moderate, 1; mild, 3.

Progress of the disease. Duration of pyrexia. In those who were pyrexial temperature remained elevated for two to five days.

Stools. The stools became normal in one to twenty-three days (average six days).

Dehydration. This was severe in five cases and intravenous fluids were given.

Weight. All but the infant who died gained weight satisfactorily.

Bacteriology. Faeces were examined in all cases with negative result in eight. One grew B. Morgan No. 5.

Complications of the illness. Three infants developed otitis media, one on the eleventh day, one on the thirteenth day and one on the thirty-first day in hospital.

Post-mortem examination was unfortunately refused.

Comment

This group of gastroenteritis in older infants is small chiefly owing to the difficulty of finding infants not manifesting some signs of parenteral infection. The sulphasuxidine group seems to be the mildest of the three. There is little difference in the results in the three groups and the impression has been gained that the essential and most urgent aspect of the treatment is adequate treatment of dehydration. Some of the cases gained weight while having the drugs but it is felt that this is due to overcoming the dehydration and not to any virtue of the drugs. The group is too small to allow of a valid pronouncement and further investigation of this type of case is required.

Part II

(2) Parenteral infections

(a) **Pneumonia and bronchopneumonia.** This group contains 97 cases and four sulphonamides were used, sulphamezathine, sulphathiazole, sulphadiazine and sulphapyridine. It is not necessary to describe in detail the symptoms which this group presented. The great majority (except some of the premature infants) had cough and dyspnoea. Diarrhoea occurred in 28, vomiting in 29, pyrexia in 83 and 14 were apyrexial.

Sulphamezathine

General figures. There were 35 cases, 20 males and 15 females, among whom were eight premature infants and 27 mature infants. Thirty suffered from bronchopneumonia and five from pneumonia. Of the 35 cases, nine died (28·5 per cent.).

0 to 1 month, 14; 7 deaths (50 per cent.).

1 to 9 months, 21; 2 deaths (9 per cent.).

General assessment. Severe, 23 with 9 deaths (39·1 per cent); moderate, 12 with no deaths.

Progress of the disease. Duration of pyrexia. In nine cases temperature was normal in 24 hours, six in 48 hours, five in 72 hours, one in four days, one in six days, one in ten days and one in seventeen days. In five pyrexia was uncontrolled.

Cough and dyspnoea. In seventeen marked improvement took place in 24 to 48 hours. In the nine fatal cases the dyspnoea was not relieved. Five of the older infants who had whooping-cough improved slowly and five who were extremely ill on admission took several days to settle.

Stools. In those who had diarrhoea and recovered, stools were normal in one to four days.

Total dose of the drug. Average 14 gm.

Complications of the drug. Four cases in the neonatal group developed a mild cyanosis which was thought possibly due to the drug. This disappeared on stopping the drug and no other complications took place.

Complications of the illness. In the neonatal group there was one case of rhinitis, one of submaxillary abscess and one of mastitis. Among the older infants five had whooping-cough, three had otitis media on admission and two developed it while in hospital. One infant with lobar pneumonia developed extensive cavitation of the right lung which eventually resolved almost completely. Unfortunately he was removed against advice after eight weeks in hospital.

Post-mortem findings. Permission for post-mortem examination was obtained in eight of the nine deaths. In six cases the presence of bronchopneumonia was confirmed. Of the remaining two, one was found to have bilateral acute otitis media and the other bilateral mastoiditis, in addition to bronchopneumonia.

Sulphathiazole

General figures. There were 28 cases, 21 males and seven females including three premature infants and 25 mature infants. Twenty-five suffered from bronchopneumonia and three from pneumonia. Of the 28 cases, 11 died (39·2 per cent.).

0 to 1 month, 10; 6 deaths (60 per cent.).

1 to 9 months, 18; 5 deaths (27·7 per cent.).

General assessment. Severe, 20 with 11 deaths (55 per cent.); moderate, 8 with no deaths.

PROGRESS OF THE DISEASE. Duration of pyrexia. One was apyrexial throughout. One was pyrexial for one day, four for two days, three for three days, four for four days, one for five days, one for eight days, one for twelve days and one for 44 days. The latter had two courses of treatment and ultimately recovered. In eleven cases temperature was uncontrolled.

Cough and dyspnoea. The great majority had cough and dyspnoea which improved in varying periods from 24 to 72 hours except those suffering from whooping-cough.

Stools. Stools became normal in two to five days except in one infant who had diarrhoea for six days and required intravenous fluids.

TOTAL DOSE OF THE DRUG. Average 17·5 gm. No complications of the drug were observed.

COMPLICATIONS OF THE ILLNESS. Four infants had otitis media on admission and one required mastoidectomy. Two developed otitis media while in hospital. One suffered from measles and two from whooping-cough. One mongoloid defective had jaundice.

POST-MORTEM FINDINGS. Post-mortem examination was obtained in only five of the eleven patients who died. One showed pneumonia, one bronchopneumonia, one bronchopneumonia and left acute otitis media, one pneumonia and empyema, and one bronchopneumonia with right-sided mastoiditis.

SULPHADIAZINE

GENERAL FIGURES. There were 15 patients, 11 males and 4 females; 3 were premature and 12 were mature infants. Thirteen suffered from bronchopneumonia and 2 from pneumonia. Of the 15 cases, 7 died (46·6 per cent.).

0 to 1 month, 7; 3 deaths (42·8 per cent.).

1 to 9 months, 8; 4 deaths (50 per cent.).

GENERAL ASSESSMENT. Severe, 9 with 7 deaths (77·7 per cent.); moderate, 6 with no deaths.

PROGRESS OF THE DISEASE. Duration of pyrexia. Of the survivors four were apyrexial throughout. One was pyrexial for 24 hours, two for 48 hours and one for six days. In those who died, two premature infants were apyrexial throughout, one premature infant was pyrexial for 24 hours only, one infant for four days and in three cases the temperature was uncontrolled.

Cough and dyspnoea. In ten improvement occurred in 24 to 72 hours. In one which had whooping-cough dyspnoea improved in 48 hours but cough persisted.

Stools. In those with diarrhoea, stools were normal in one to four days.

TOTAL DOSE OF THE DRUG. Average 15·5 gm. No complications of the drug were observed.

COMPLICATIONS OF THE ILLNESS. One had otitis media on admission, one developed it while in hospital and one had congenital heart disease.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in six cases with the following results:—

1. Bronchopneumonia, congenital heart disease with subacute infective endocarditis.
2. Bronchopneumonia, pericardial and pleural effusions and right mastoiditis.
3. Pneumonia, bilateral otitis media, patent foramen ovale.
4. Bronchopneumonia, atelectasis and prematurity.
5. Bronchopneumonia and right mastoiditis.
6. Bronchopneumonia and prematurity.

SULPHAPYRIDINE

GENERAL FIGURES. There were 19 cases, eight males and eleven females. All were mature infants. Fifteen suffered from bronchopneumonia and four from pneumonia. Of the 19 cases, six died (31·5 per cent.).

0 to 1 month, 7; 3 deaths (42·8 per cent.).

1 to 9 months, 12; 2 deaths (16·6 per cent.).

GENERAL ASSESSMENT. Severe, 10 with 5 deaths (50 per cent.); moderate, 9 with no deaths.

PROGRESS OF THE DISEASE. Duration of the pyrexia. Five patients were apyrexial in 24 hours, one in three days, three in four days, four in six days, one in 15 days. In five cases temperature was uncontrolled.

Cough and dyspnoea. These symptoms continued for varying times but on the whole longer than with sulphamezathine and sulphadiazine.

Stools. In those with diarrhoea, stools became normal in two to ten days.

TOTAL DOSE OF THE DRUG. Average 14·2 gm.

COMPLICATIONS OF THE DRUG. Four patients were very cyanosed due to the drug and one vomited frequently until the drug was stopped.

COMPLICATIONS OF THE ILLNESS. One patient had bilateral acute otitis media with profuse otorrhoea on admission. Two developed otitis media in hospital and myringotomy was necessary. One of these also developed chicken pox. In one case the pneumonia relapsed and was successfully re-treated. Another patient developed a small abscess on the right shoulder which had to be incised and one was being treated with sulphapyridine for gonorrhoeal ophthalmia when the pneumonia commenced.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in four cases with the following results:

1. Bronchopneumonia with pericardial effusion and grossly enlarged heart.
2. Bronchopneumonia.
3. Bronchopneumonia and right acute otitis media.
4. Pneumonia, left upper and lower lobes.

Comment

TABLE 2

	Mezathine 35 cases		Thiazole 28 cases		Diazine 15 cases		Pyridine 19 cases	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Premature ..	8	22·8	3	10·7	3	20·0	—	—
Neonates ..	14	40·0	10	35·7	7	46·6	7	36·8
Severe	23	65·7	20	71·4	9	60·0	10	52·6
Moderate ..	12	34·3	8	28·6	6	40·0	9	47·4
Deaths	9	28·5	11	39·2	7	46·6	6	31·5

From table 2 it will be seen that the four groups are not quite equal in severity. Having regard to the factors which influence the severity of the groups from the therapeutic point of view and beginning with the most severe, the groups probably arrange themselves in order of severity as follows — sulphamezathine group, sulphadiazine

group, sulphathiazole group and sulphapyridine group. It is striking that the lowest death rate occurs in the most severe group, which was treated with sulphamezathine. As it happens the mildest group was treated with sulphapyridine and here the death rate is slightly higher than in the most severe group. In the sulphathiazole group the high incidence of severe cases is to some extent offset by the lower incidence of prematurity and neonates, and in the sulphadiazine group the higher incidence of prematurity and neonates is offset to some extent by the lower incidence of severe cases. Sulphathiazole seems to give rather better results than sulphadiazine, and the lowest death rate among the severe cases is in the sulphamezathine group. From this analysis it would seem justifiable to assess the merits of the various drugs in descending order as follows—sulphamezathine, sulphathiazole, sulphapyridine and sulphadiazine. Under one month the death rate is high with all the drugs, i.e. 40 to 60 per cent. Therefore the difference in the total therapeutic result appears to occur among the older infants. Comparing the average total dose it is found that smaller amounts of sulphamezathine and sulphapyridine are required to achieve their results than is the case with the others. Sulphamezathine was found to be well tolerated, non-toxic and to give rapid and satisfactory results. In the neonatal group four cases displayed a mild cyanosis, which (in three who recovered) continued after the acute phase was over and only ceased when the drug was discontinued. This cyanosis was thought to be due to the drug but is not a contraindication to its use. With sulphathiazole the response seemed to be slower, but no toxic manifestations occurred either with sulphathiazole or with sulphadiazine. Sulphapyridine produced more severe toxic results than the others, four becoming very cyanosed and one vomiting frequently. It was also thought that cough and dyspnoea continued longer than with the other drugs. From this series it seems that sulphamezathine is the drug of choice.

Jennings and Patterson (1942) describe eleven cases, nine of whom were under two years of age, all of whom improved in thirty-six hours and all of whom recovered. One relapsed and was successfully re-treated. They also describe satisfactory response in older children. One infant developed a rash after 7 gm. of sulphamezathine and two older children developed rashes, but no other toxic effects were observed. Peters and Easby (1943) describe their experience of sulphamezathine in a group of cases containing 21 patients under two years of age, of whom two died. One child aged two had complete urinary suppression and two others developed 'a curious painless brawny oedema of the whole legs and arms' thought to be due to some circulatory disturbance. Apart from this they report no toxic effects. Experience of the treatment of pneumonia in older subjects with sulphathiazole is described by Gaisford and Whitelaw (1940) who found that the temperature did not fall so rapidly as with sulphapyridine. Greengard, Raycroft and Motel (1941), describe 200 infants treated with sulphapyridine with a 10 per cent. mortality. Before chemotherapy their death rate was 32 per cent. In an addendum to their paper Evans and Gaisford (1938) mention forty cases of bronchopneumonia in children treated with sulphapyridine with two deaths. They also mention two infants who recovered. Gaisford, Whitelaw and Evans (1939) describe six infants suffering from pneumonia and bronchopneumonia treated with parenteral sulphapyridine soluble, administered intra-muscularly with two deaths.

(2) Parenteral infections

(b) **Bronchitis and upper respiratory infection.** In this group there are forty cases and the same sulphonamides were used. Symptoms were as follows: All showed some cough and dyspnoea. Diarrhoea occurred in seven, vomiting in 15. Pyrexia was present in 27, while 13 were apyrexial.

Sulphamezathine

General figures. There were 17 cases, ten males and seven females, among whom there were no deaths.

General assessment. Severe, 5; moderate, 11; mild, 1.

Progress of the disease. Duration of pyrexia. Six were apyrexial in 24 hours, four in 48 hours, one in 96 hours, whilst six were apyrexial throughout. Cough and dyspnoea lasted for varying periods. Vomiting ceased in 24 to 96 hours. Only one gave a history of diarrhoea but the stools were found to be normal after admission.

Total dose of the drug. Average 10 gm. No complications of the drug were noted.

Complications of the illness. One had bilateral otitis media on admission and four developed this complication from the tenth to twenty-first day in hospital. Four of these required myringotomy. In two cases the otitis media was treated with different sulphonamides—sulphadiazine and sulphathiazole respectively. They all made good recoveries.

Suphathiazole

General figures. There were seven cases, five males and two females and two were premature infants. No deaths occurred.

General assessment. Severe, 1; moderate, 5; mild, 1.

Progress of the disease. Duration of pyrexia. Temperature fell in 24 hours in three cases, and in 48 hours in one case. Three were apyrexial throughout. Of the five giving a history of vomiting, three did not vomit after admission and two ceased in 24 hours. Of the three with diarrhoea, stools became normal in 24 hours in one case and in 48 hours in two cases. One was slightly dehydrated on admission but this was relieved in 24 hours.

Total dose of the drug. Average 14 gm. There were no complications.

Complications of the illness. One case relapsed on the nineteenth day and was successfully re-treated, the temperature falling in 24 hours on both occasions. One had bilateral otitis media on admission and one developed it on the seventeenth day.

Sulphadiazine

General figures. There were five cases, two males and three females, of whom one died.

General assessment. Moderate, 2; mild, 3.

Progress of the disease. One was apyrexial in 24 hours, one in 48 hours and one in five days. Two were apyrexial throughout. There was nothing noteworthy about the other symptoms.

TOTAL DOSE OF THE DRUG. Average 16·25 gm. No complications were noted.

COMPLICATIONS OF THE ILLNESS. One had a cleft palate and one had a septic finger A third developed bilateral acute otitis media on the twelfth day. This infant, who died, required myringotomy and intravenous fluids.

POST-MORTEM FINDINGS. Pus was found in the right mastoid antrum and in the left middle ear. Further examination was not permitted.

SULPHAPYRIDINE

GENERAL FIGURES. There were 11 cases, five males and six females, among whom were two premature infants. Two deaths occurred.

GENERAL ASSESSMENT. Severe, 5; moderate, 6.

PROGRESS OF THE DISEASE. Four were apyrexial in 24 hours, one in 48 hours, two in 72 hours and one in 96 hours. In one case, a premature infant who died, temperature was uncontrolled. Other symptoms presented no remarkable features.

TOTAL DOSE OF THE DRUG. Average 16 gm. The premature infant who died only had 1·0 gm. but the other case who died had 13·5 gm. There were no complications of the drug.

COMPLICATIONS OF THE ILLNESS. One case developed otitis media on the sixteenth day. Another who died had left acute otitis media on admission and the right became similarly affected on the sixteenth day. Intravenous therapy and blood transfusions failed to help and ultimately bilateral mastoidectomy was performed when much pus was found in both antra. The pus was found to be sterile. Unfortunately the infant died, and permission for post-mortem examination was refused.

POST-MORTEM FINDINGS. Permission in the case of the premature infant was obtained and the diagnosis of bronchitis and prematurity confirmed.

Comment

This was on the whole a mild group of cases and it is felt that the great majority would have progressed just as favourably without sulphonamides. There were three deaths, two of them due, not to bronchitis, but to the development of otitis media and mastoiditis. The third was an infant in whom prematurity played as great a part as the bronchitis. Cases of bronchitis and upper respiratory infection, especially the latter, are peculiarly prone to develop otitis media. Eight cases (20 per cent.) developed this complication and it seems that the exhibition of sulphonamides has little effect in preventing the onset of this serious complication.

Part III

(2) Parenteral infections (*continued*)

(c) Otitis media and mastoiditis. In this group 97 cases are described and four sulphonamides are used—sulphadiazine, sulphamezathine, sulphathiazole and sulphapyridine. A few cases received no chemotherapy. The group presented symptoms as follows—diarrhoea 72, vomiting 64, dehydration 76, weight loss 85 and pyrexia 67, with signs of inflammation in the tympanic membranes or otorrhoea in all cases.

SULPHADIAZINE

GENERAL FIGURES. There were 32 cases, 19 males and 13 females, among whom were 5 premature infants and 27 mature infants. No deaths occurred. Twenty-two were neonates and 10 were older infants.

GENERAL ASSESSMENT. Severe, 12; moderate, 5; mild, 15.

PROGRESS OF THE DISEASE. Duration of pyrexia. Fifteen cases were apyrexial throughout. In the remainder the temperature varied from 99° F to 103° F. and lasted on an average three days. In those with diarrhoea stools became normal in an average of 3·8 days. In twelve cases dehydration was overcome by glucose saline by mouth, one received subcutaneous and intramuscular salines and five required continuous intravenous fluid. With the exception of three taken from hospital against advice, all ultimately gained weight. Only one case relapsed and was successfully retreated.

TOTAL DOSE OF THE DRUG. Average 17 gm. No complications were noted.

LOCAL TREATMENT. Twenty-eight cases received local treatment with glycerin and carbolic acid drops and a few, when otorrhoea persisted, received spirit drops.

SULPHAMEZATHINE

GENERAL FIGURES. There were 12 cases, 11 males and one female, who were all mature infants and none was in the neonatal period of life. Of the 12 cases, one died (8·5 per cent.).

GENERAL ASSESSMENT. Severe, 7 with 1 death; moderate, 4; mild, 1.

PROGRESS OF THE DISEASE. Vomiting. Of those giving a history of vomiting, two did not vomit after the commencement of the treatment. The others continued to vomit for periods varying from two to six days, average three days.

Diarrhoea. Of those giving a history of diarrhoea the diarrhoea continued for periods varying from two to nine days (average four days) after the commencement of treatment.

Dehydration. This was overcome by fluids by mouth in nine cases. One infant was given subcutaneous salines and the other two continuous-intravenous drip salines.

Weight loss. With the exception of the infant who died and one taken home against advice, all ultimately gained weight.

Pyrexia. Two were apyrexial throughout. The remainder had temperatures varying from 100·8° F. to 104·5° F. which continued from two to eight days, average four days.

Relapse. Three cases relapsed and myringotomies became necessary. One of these appeared to have settled without perforation, but later myringotomy became necessary. In the case which died myringotomy was performed and the ears discharged, but the infant did not respond and was thought to be probably suffering from mastoiditis. Unfortunately permission for post-mortem examination was refused.

TOTAL DOSE OF THE DRUG. Average 17 gm. No complications were noted.

LOCAL TREATMENT. Glycerin and carbolic acid drops were given in all cases.

SULPHATHIAZOLE

GENERAL FIGURES. There were 35 cases, 19 males and 16 females, among whom were three premature infants and 32 mature infants. Of the 35 cases, eight died (22·8 per cent.).

0 to 1 month, 9; 3 deaths (33·3 per cent.).

1 to 9 months, 26; 5 deaths (19·2 per cent.).

GENERAL ASSESSMENT. Severe, 16 with 8 deaths (50 per cent.); moderate, 18 with no deaths; mild, 1 with no deaths.

PROGRESS OF THE DISEASE. Vomiting continued on an average for two days.

Diarrhoea continued for 2 to 21 days (average five days).

Dehydration. This was overcome by fluids by mouth in twenty cases. Fifteen required continuous intravenous drip salines.

Weight loss. Of those who recovered the majority gained weight. One was taken from hospital against advice and some could not be weighed as they suffered from some infectious disease, e.g. whooping-cough.

Pyrexia. Seven were apyrexial throughout and the remainder were pyrexial for one to four days, average 2·5 days.

Relapse. Only one case relapsed and was subsequently successfully treated with penicillin.

TOTAL DOSE OF THE DRUG. Average 16 gm. No complications were noted.

LOCAL TREATMENT. Thirty cases had glycerin and carbolic acid drops and local heat.

POST-MORTEM FINDINGS. Unfortunately permission was obtained only in two cases. In one of these pus was found in both middle ears and mastoid cells and severe bronchopneumonia. In the second case much bronchitis was found but the middle ears seemed clear. Myringotomy had released thin pus from the left middle ear in this case and it is possible that chemotherapy had caused resolution of the otitis media. In all the other cases who died myringotomy had released considerable quantities of pus and in one the ears had apparently resolved, but the infant was thought to have died of pemphigus and septicaemia. The two cases upon whom mastoidectomies were performed died. Pus was found in both antra in these cases.

SULPHAPYRIDINE

GENERAL FIGURES. There were six cases, four males and two females. All were mature infants and there were three deaths. There was one neonate which recovered.

GENERAL ASSESSMENT. Severe, 4 with 3 deaths (75 per cent); moderate, 2.

PROGRESS OF THE DISEASE. Vomiting ceased in 24 to 48 hours in those who recovered.

Diarrhoea continued for two to seven days.

Dehydration. One was not dehydrated. In one dehydration was overcome by fluids by mouth and one required continuous intravenous drip saline.

Weight loss. Those who recovered gained well.

Pyrexia. Two were apyrexial and once ceased to be so after 48 hours.

Relapse. No relapses occurred in those who recovered.

TOTAL DOSE OF THE DRUG. In those who recovered the average was 13 gm. No complications of the drug were observed.

LOCAL TREATMENT. All had glycerin and carbolic acid drops and local heat.

Three cases died, all of whom ultimately required myringotomy. Two originally discharged spontaneously after the drug had been begun and improved, but later became ill again when myringotomy was necessary and pus released. These cases had three courses of sulphapyridine with a total dose of 52·5 gm. and 34·5 gm. respectively, i.e. relapse after apparent recovery occurred. In one case bilateral mastoidectomy was performed and pus found in both antra. No post-mortem examinations were obtained and one of these cases developed severe chicken pox.

NO CHEMOTHERAPY

GENERAL FIGURES. There were twelve cases, five males and seven females, among whom was one premature infant. Two were in the neonatal period, of whom one died. Ten were older infants. Of the twelve cases, two died.

GENERAL ASSESSMENT. Severe, 4 with 2 deaths (50 per cent.); moderate, 6; mild, 2.

PROGRESS OF THE DISEASE. Vomiting ceased in one to three days.

Diarrhoea. Four had no diarrhoea after the commencement of treatment. One had diarrhoea for seven days but the others continued with periods of diarrhoea for three to seven weeks, progress being very slow.

Dehyration. All except one received fluids by mouth. Of the two who died one received fluids by mouth and the other continuous intravenous drip saline.

Weight loss. All of those who recovered, except one, gained weight satisfactorily.

Pyrexia. Seven were apyrexial throughout. The others were pyrexial for one to four days, average two days.

LOCAL TREATMENT. Eleven had glycerin and carbolic acid drops and local heat.

POST-MORTEM EXAMINATIONS. Permission for examination was obtained in the two cases who died. In one, a premature infant, from whose ears pus had been obtained by myringotomy, bronchopneumonia and pus in the left middle ear were found. The second case had been admitted with pneumonia which had improved when the otitis media developed. Permission for a complete examination was withheld and only the mastoids were opened. Pus was found in both antra.

Comment

The difficulties in assessing the value of the sulphonamides used are apparent from a study of tables 3 and 4. In table 3 it can be seen that from the point of view of the incidence of prematurity the sulphadiazine group is the most severe. From the point of view of the severity of the illness the groups, unfortunately headed by the two smallest groups, fall into the following order—sulphapyridine, sulphamezathine, sulphathiazole, sulphadiazine and the group with no chemotherapy. Although the group with no chemotherapy is the least severe, the results in this group are not so good as in the sulphamezathine and sulphadiazine groups, the former being one of the most severe groups and the latter containing the highest percentage of premature infants. Sulphapyridine gives the worst results of the drug-treated groups. If the first three are

arranged according to severity and results the following two columns can be obtained.

Severity	Results
Sulphamezathine	Sulphadiazine
Sulphathiazole	Sulphamezathine
Sulphadiazine	Sulphathiazole

The drug which keeps highest in both columns is sulphamezathine, which would therefore seem to be the most efficacious drug. Sulphadiazine and sulphathiazole take second place. Unfortunately the sulphamezathine group is a small group and this conclusion is probably not justifiable. On the other hand table 4 reveals that in the sulphamezathine group a high proportion of cases required myringotomy after the drug had been given and in no case did the otitis media settle without discharging. In assessing table 4 the stage which the otitis media had reached when treatment was instituted must be kept in mind. For instance, in the sulphathiazole group a large number of myringotomies were performed simultaneously with administration of the drug because there was obviously pus behind the drums when treatment was begun. Nevertheless the sulphathiazole group contains the highest percentage which settled without discharge of pus and the lowest percentage of those which were given a chance to settle and failed to do so without myringotomy. No spontaneous discharge occurred in the sulphathiazole group but these good points are offset by the higher death rate. From this point of view the next most satisfactory drug is sulphadiazine, in which group no deaths occurred. Clinically sulphathiazole seemed to have a good effect on the amount of discharge after the necessary myringotomies had been performed and a similar effect was noticed with sulphapyridine. With sulphadiazine there was much less tendency to relapse than with sulphamezathine and the effect of this drug on the general condition and the tympanic membranes was better than with sulphamezathine. Sulphamezathine seemed to exert an improvement on the toxicity of the infants but its local effect on the drums was less than with sulphathiazole or sulphadiazine. From this analysis it

Table 3

	Diazine 32 cases		Mezathine 12 cases		Thiazole 35 cases		Pyridine 6 cases		No chemotherapy 12 cases	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Premature.. ..	5	15·6	—	—	3	8·5	—	—	1	8·3
Mature	27	84·3	12	100·0	32	91·4	6	100·0	11	91·6
Mild	15	46·8	1	8·3	1	2·8	—	—	2	16·6
Moderate	5	15·6	4	33·3	18	51·4	2	33·3	6	50·0
Severe	12	37·5	7	58·3	16	45·7	4	66·6	4	33·3
Deaths	—	—	1	8·3	8	22·8	3	50·0	2	16·6

Table 4

Drug	No discharge	Aural discharge						Relapse rate	Mastoidectomies	Deaths
		Myringotomy			Spontaneous discharge					
		Before drug	Simul. with drug	After drug	Before drug	Simul. with drug	After drug			
Diazine .. .. (32 cases)	6 (18·7)	1 (3·1)	7 (21·8)	5 (15·6)	8 (25·0)	3 (9·3)	2 (6·2)	1 (3·1)	2 (6·2)	—
Mezathine .. (12 cases)	—	1 (8·3)	2 (16·6)	7 (58·3)	—	1 (8·3)	1 (8·3)	3 (25)	3 (25·0)	1 (8·3)
Thiazole .. .. (35 cases)	7 (20·0)	3 (8·5)	21(60·0)	4 (11·2)	—	—	—	1 (2·8)	2 (5·7)	8 (22·8)
Pyridine .. .. (6 cases)	1 (16·6)	—	3 (50·0)	2 (33·3)	—	—	—	2 (33·3)	1 (16·6)	3 (50·0)
		Myringotomy			Spontaneous discharge					
No chemotherapy (12 cases)	1 (8·3)	11 (91·6)			—			2 (16·6)	—	2 (16·6)

(Percentages in brackets)

seems that the best drugs to employ in otitis media of infancy are sulphathiazole and sulphadiazine.

There are few references describing specifically the effect of sulphonamides in otitis media and mastoiditis in infancy. Burns and Gunn (1944) describe four cases of gastroenteritis associated with otitis media and mastoiditis treated with sulphonamides, one, which recovered, with sulphathiazole and three, one of whom died, with sulphamezathine. These cases also received penicillin either locally or systemically so that it is difficult to assess the part played by the sulphonamides. Leathart (1943) mentions the use of sulphonamides but gives no details or impressions. Patterson and Stewart Smith (1944) say that many of their cases were treated with 'adequate doses of one or other of the sulphonamide drugs' but no effect was observed. In a series of 124 cases of infantile diarrhoea and vomiting Alexander and Eiser (1944) found 60 cases of otitis media and in describing their treatment say that after search for foci of parenteral infection 'sulphonamides, chiefly sulphathiazole, were given in large doses' but again no details or impressions of the efficacy of this treatment are given.

Another interesting point deserves mention. Some otologists, for example Dingley (1944), find that the administration of sulphonamides to older children and adults may lead to masking of serious intracranial complications with disastrous results. This fear need not arise in connexion with infantile otitis media and mastoiditis because intracranial complications are rare. This has been the experience of Southby (1924), and Dodds (1931), describing a case of infantile mastoiditis which developed purulent meningitis, also comments upon the rarity of intracranial complications. Patterson and Stewart Smith (1944) state that 'subperiosteal abscess should be, and in fact is, a very common complication of mastoiditis in babies' and that 'extradural abscess and meningitis are ever present dangers, and not rare complications, of acute otitis media in infants.' This is not in keeping with the experience of the present writers. Patterson and Stewart Smith also open their description of their investigation by using the term 'mastoid' to include the middle ear and mastoid antrum and state that under the age of two years there is no sharp division between them and the mastoid cells are undeveloped. We strongly disagree with this view, holding that otitis media can undoubtedly occur alone and unaccompanied by mastoiditis in infancy. Infantile mastoiditis is probably uninfluenced by sulphonamides but acute otitis media can certainly be influenced, although not to the extent we should wish.

(2) Parenteral infections

(d) **Pyelitis.** There were seven cases in this group, one male and six females. All were mature and one was in the neonatal period. One death occurred. Symptoms were as follows—vomiting occurred in three cases, diarrhoea in all the cases, dehydration in five, pyrexia in five varying from 100·2° to 104° F., weight loss in three cases. Three cases were judged severe, two moderate and two mild. All were B. coli infections. Sulphapyridine, sulphathiazole, sulphadiazine and sulphamezathine were employed and one case received no chemotherapy.

Progress of the disease

(1) Case treated with sulphapyridine. This was a case of intussusception which developed pyelitis during the third week in hospital. Urinalysis showed albumin and pus (20 cells per field). This case made an uneventful recovery, having received 16 gm. of the drug.

(2) Cases treated with sulphathiazole. (a) This infant was admitted to hospital with pyelitis. Urinalysis showed albumin and pus (110 cells per field). This infant made a good recovery, having had 22 gm. of the drug.

(b) This infant was admitted as a feeding error and in the third week in hospital developed pyelitis. With the first course of sulphathiazole improvement and gain in weight occurred but the urine still contained pus. Relapse followed and a second course was commenced but ultimately the infant died. Urinalysis showed albumin and pus (20 to 25 cells per field persistently), hyaline and granular casts. The blood urea was 49 mgm. per cent. The first course consisted of 28 gm. of the drug, but on the second occasion the infant only survived long enough to have 7 gm.

Post-mortem findings. Pus was found in the pelves of both kidneys. There were no congenital malformations.

(3) Case treated with sulphamezathine. This infant, who was admitted with pyelitis, was very ill and dehydrated and required a continuous intravenous drip saline. Urinalysis—albumin and pus (20 cells per field) and organisms were still present in the urine after the drug was stopped. This infant recovered, having had 18 gm. of the drug.

(4) Case treated with sulphathiazole and sulphadiazine. This infant was admitted with bilateral acute otitis media and developed pyelitis during the third week in hospital. A course of sulphathiazole was given but pus remained in the urine although improvement and gain in weight were satisfactory. Relapse then occurred and a course of sulphadiazine was given, after which the urinary infection resolved rapidly but the urine was much less heavily infected than during the sulphathiazole course. Urinalysis, during and after sulphathiazole, showed a considerable quantity of albumin and pus (180 to 250 cells per field) and at the commencement of the sulphadiazine course, a trace of albumin and pus (30 cells per field). Blood urea at commencement of the second course was 42 mgm. per cent. This infant made a good recovery, having had 19 gm. of sulphathiazole and 20 gm. of sulphadiazine.

(5) Case treated with sulphamezathine and sulphathiazole. This infant was admitted with pyelitis for which a course of sulphamezathine was given. Although improvement and gain in weight occurred, pus remained in the urine and relapse occurred during the fourth week in hospital when a course of sulphathiazole was given. Urinalysis showed albumin and pus (20 to 30 cells per field). Recovery eventually took place, the infant having had 20 gm. of sulphathiazole and 21 gm. of sulphamezathine.

(6) Case treated with sodium citrate and no sulphonamide. This infant was admitted as a case of feeding error and great difficulty was experienced in finding a suitable feed. Urine examination was negative shortly after admission. During the eighth week in hospital pyelitis developed

and 5 grains sodium citrate with 5 grains sodium bicarbonate were administered four-hourly for nine days. Urinalysis showed albumin and pus (40 cells per field). With this treatment the urine cleared in six days.

Comment

Owing to the small number of cases it is difficult to compare the different sulphonamides. The only case treated with sulphadiazine made a rapid recovery although there had been a severe infection previously treated unsuccessfully with sulphathiazole. On the other hand the case treated with alkalies alone made an equally rapid recovery. Three cases relapsed and in these the urine had never cleared completely. Although it is not always possible to obtain a daily specimen in infants, some indication of the efficacy of these drugs may be obtained by comparing the times taken for the urine to become normal. With sulphapyridine this took seven days. Sulphathiazole was used on four occasions; the urine became normal in four and eight days respectively in two of the cases but was unaffected in the other two. With sulphadiazine the urine became clear in eight days but was possibly helped by the previous course of sulphathiazole. Sulphamezathine was used on two occasions and in one the urine took thirty-two days to become clear and in the other it was unaffected. The urine cleared in six days in the case treated with alkalies only. These results are inconclusive and further observation is necessary. Burns and Gunn (1944) report a case of B. coli pyelitis which responded well to sulphathiazole.

(2) Parenteral infections

(e) **Skin sepsis.** This group contains a small number of cases of skin sepsis, 22 in all.

Sulphadiazine

This group contains six cases suffering from various forms of skin sepsis, two premature infants and four mature infants of whom one lost weight and five were stationary. Four were pyrexial for one to six days. All recovered and the average amount of sulphadiazine given was 15 gm. Two were judged severe, one moderate and three mild.

Description of cases

(1) Cellulitis of abdomen and pubis—very satisfactory response.
(2) Abscess of chin and spreading cellulitis—apparently settled then recurred and had to be incised.
(3) Cellulitis of cheek—ultimately settled but response poor.
(4) Cellulitis of cheek—satisfactory response.
(5) Umbilical sepsis—satisfactory response.
(6) Submaxillary abscess—no effect, required incission later.

Sulphathiazole

There are five cases of skin sepsis in this group, which contains two premature infants and three mature infants. Two lost weight, two were stationary and one continued to gain. Four were pyrexial and in the two premature infants this was uncontrolled. In the other two cases temperature continued five and twelve days respectively. The two premature infants died. Two received two courses of the drug and the average amount given was 13 gm. Four were judged severe and one moderate.

Description of cases

(1) Cellulitis of face—responded well, relapsed and was successfully retreated.
(2) Multiple septic spots—these occurred on abdomen and legs and one had to be incised—no response, died.
(3) Multiple septic spots with surrounding inflammation—no response, died.
(4) Abscess of wrist and multiple septic spots (Staph. aureus)—abscess was incised and the drug exerted some effect.
(5) Abscess of foot (Staph. aureus)—incisions were carried out and two courses of the drug given—response poor.

Post-mortem findings. Permission was obtained in one case which died. The sepsis seemed to be healing but the lungs showed much bronchitis.

Sulphonamide cream

The cases in this group were treated with sulphonamide cream (5 per cent. sulphanilamide) applied locally. Five also had small amounts of sulphadiazine by mouth. The group consists of eleven infants among whom were three premature infants. Four lost no weight, three were stationary, two lost weight and two became too ill to be weighed. Only two were pyrexial, uncontrolled in one who died and lasting four days in the other. Of the eleven cases four died, two of these being premature infants. Three were judged severe, four moderate and four mild.

Description of cases

Seven were thought to be pemphigus and in five of these staphylococcus aureus was grown from the blebs. There was one death, a premature infant. The remaining four were cases of septic spots affecting mainly the face and scalp. One also had right mastitis which required incision. There were three deaths, one a premature infant. Staphylococcus was grown in two of these cases. In the pemphigus group the response was good, the condition being much improved in two to four days and healed in six to thirteen days. In the case which died the eruption was extensive and no apparent effect took place. It will be noticed that only three cases were considered severe although four died. In the remaining infant who died the skin sepsis was mild and as post-mortem examination was refused the exact cause of death is not known.

Post-mortem findings. Permission was obtained only in one case, the pemphigus who died, In addition to the pemphigus and prematurity bronchopneumonia affecting both lower lobes was found.

Comment

In the sulphadiazine group a satisfactory response took place when there was no pus formation and when discharge of pus was free. But in the presence of an actual abscess no response was observed. The sulphathiazole group was more severe, but nevertheless the response was not so good as with

sulphadiazine. The local treatment of pemphigus with sulphonamide cream is usually very satisfactory but in the scalp type of infection described the response was poor. Troup and White (1939) described one case of pemphigus, treated with sulphapyridine by mouth, which was cured in five days.

Discussion

In addition to the comments at the end of each section, certain general considerations deserve mention. The success of treatment depends partly upon accurate diagnosis, and the difficulties of diagnosis in infancy are well known. In attempting to assess the results of treatment the attitude of the clinician with regard to the interpretation of clinical signs exerts a great influence. Parenteral infection is common and is responsible for many symptoms which have hitherto been ascribed to quite other causes. The term 'gastroenteritis' is often used incorrectly, since evidence of parenteral infection can so often be found; the main difficulty in diagnosis is the crudeness of methods of clinical examination. We believe that certain forms of parenteral infection give rise to a symptomatic diarrhoea and vomiting with accompanying dehydration. Others take the view that the illness begins as an enteral infection of obscure etiology and that parenteral infection is a secondary phenomenon. In such cases, e.g. otitis media and mastoiditis, the type of treatment, and therefore its success or failure, depends upon which of these views is the correct one. It may be suggested that the figures described in the present series constitute a strong argument against the parenteral theory of etiology (see table 5). Assuming for the purpose of discussion that the parenteral theory is the true one, why is the incidence of diarrhoea and vomiting in the pneumonia and bronchitis groups so much less than in the others? This is a difficult question to answer and various factors are involved. (1) The general state of health of the infant at the time when it is assailed by the infection is of great importance. (2) Infants, no less than adults, show individual differences and some manifest greater hydrolability than others. As Alexander and Eiser (1944) put it, 'Quite often the whole clinical picture is most suggestive of an upset caused by some trigger mechanism setting up the disproportionately violent reaction of diarrhoea and vomiting which eventually marches on its way to a fatal outcome, regardless of the triviality of the first provoking factor.' In other words the trigger is more easily pressed in some than in others. (3) Diarrhoea and vomiting are commoner in some infections than in others and this seems to depend on the site of the infection. The more 'enclosed', if such an expression can be used, the infection is the more likely are these symptoms to occur, e.g. otitis media, mastoiditis and pyelitis. These theories may seem rather far-fetched but no more so than to maintain, in spite of persistently negative pathological and bacteriological findings in the gastrointestinal tract, that gastroenteritis is due to some enteral infection which has so far eluded detection. The problem is by no means settled and in assessing the results described this background must be kept in mind. The subject is worthy of much further investigation.

TABLE 5

	Diarrhoea (percentage)	Vomiting (percentage)
Neonatal gastroenteritis ..	96·8	57·8
Gastroenteritis in older infants	100·0	91·6
Pneumonia and broncho-pneumonia	28·8	29·8
Bronchitis and upper respiratory infection ..	17·5	37·5
Otitis media and mastoiditis	74·2	65·9
Pyelitis	100·0	42·8

The above arguments may apply with equal cogency to neonatal gastroenteritis, which many regard as a separate clinical entity. In the majority of the deaths in this group evidence of parenteral infection was found and it is possible that there is no real difference between the so-called neonatal gastroenteritis and gastroenteritis in older infants. Possibly the latest theory, that of a virus infection, will disprove this suggestion. The majority of virus infections are unaffected by the sulphonamides and possibly this may be an explanation of the indifferent results obtained in the present series of neonatal gastroenteritis by chemotherapy. The position of the staphylococcus aureus and organisms of the colon bacillus group in the neonatal period calls for further investigation.

Cooper, Zucker and Wagoner (1941) describe the use of sulphathiazole in acute diarrhoea and dysentery in infants and children. Their series of 123 cases contains 79 under one year. The stools of 59 (47·9 per cent.) of the 123 patients were positive for S. paradysenteriae Flexner and Sonne, and they found that sulphathiazole was of therapeutic value in those whose stools were positive but of no effect in the negative ones. No such cases were found in the present series and therefore this use of sulphathiazole has not been investigated.

The latest drug, sulphamerazine, has not yet been tried by us. In our opinion, if the infantile death rate is to be lowered, a concentrated attack upon parenteral infection is of the first importance.

Conclusions

(1) A description is given of 415 infants, suffering from various infections, the majority of patients being treated with drugs of the sulphonamide group. On the whole these drugs are well tolerated by infants.

(2) Sulphapyridine tends to cause cyanosis and vomiting. Cyanosis of mild degree but no vomiting

may also occur with sulphamezathine. Oedema occasionally occurs with sulphaguanidine and sulphasuxidine and the latter drug may also cause an increased tendency to haemorrhage.

(3) In neonatal gastroenteritis the total death rate may be reduced by the use of sulphaguanidine or sulphasuxidine but the treatment must be started early, since in severely ill cases these drugs appear to exert little effect.

(4) Sulphaguanidine and sulphasuxidine probably have little effect in gastroenteritis of older infants.

(5) In pneumonia and bronchopneumonia sulphamezathine is the drug of choice.

(6) Sulphamezathine, sulphathiazole, sulphadiazine and sulphapyridine do not produce striking results in upper respiratory infection and bronchitis. They exert little effect in preventing the development of otitis media.

(7) When otitis media occurs alone, as it often does, the sulphonamides (particularly sulphathiazole and sulphadiazine), constitute a therapeutic advance but not as great an advance as could be wished. It is felt that once mastoiditis has supervened, sulphonamides will not influence the progress of the disease.

(8) The series of pyelitis cases is too small to justify conclusions but an equally good result was obtained with sodium citrate mixture alone as with any of the sulphonamides used.

(9) Cellulitis, unaccompanied by pus formation, can be successfully treated with sulphadiazine and sulphathiazole. The local treatment of pemphigus with sulphonamide cream is very satisfactory.

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RICKETS IN SINGAPORE

BY

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Some legends die hard. 'There is no rickets in the tropics.' 'There is no rickets in Singapore.' Such remarks have been so frequently repeated that it has clouded the powers of observation. It is easy enough to produce rare cases of almost any disease, but the object of this article is to prove the prevalence of a very common disease that is responsible for a great deal of damage to child life, and to suggest the causes, and the methods of combating the condition.

Other opinions. Professor Rosedale, from the Department of Biochemistry of the College of Medicine, Singapore, basing his statements on the reports from the Medical Department for Malaya, wrote in 1934: 'Vitamin D, the anti-rachitic factor, presents no very difficult problem, as may be judged from the report of the Medical Department of the Straits Settlements for 1932, showing that out of some 50,000 admissions to Government hospitals, only two were admitted for rickets. The corresponding report for the Federated Malay States shows an admission of five cases out of some 74,000 admissions to hospital.' In 1941 Oliviero, of the same department, in 'Good Health through Feeding,' stated: 'Rickets is a comparatively rare disease in Malaya. It occurs in a mild form mainly in children of poverty-stricken parents, living in dark, insanitary cubicles.'

Kingsbury and Fasal (1940), writing from the Institute of Medical Research in Kuala Lumpur, F.M.S., found many cases of rickets in Tamil children. Miss I. M. M. Simmons, Matron of the welfare work in the rural areas of Singapore Island, recognized many cases of rickets among the children and stated as much in a report published in 1934, but the doctors did not investigate these cases.

Geography. Singapore Island is about 25 by 20 miles in extent. The town lies some three degrees north of the equator. In 1939 the population was over 700,000, of whom some 600,000 lived in the municipal area. The climate is warm and damp, the rainfall rather heavy and so regular that the island is perenially green and florid. Malaria used to be a fearful scourge, but is now well under control. The major epidemic diseases, such as cholera, plague and smallpox are now practically unknown.

Population. The Chinese represent over 80 per cent. of the population, and control most of the commerce, the coolie labour, and the farms and vegetable gardens in the rural areas. Indians, mostly Tamil labourers, but including some Sikhs and Bengal and Bombay merchants, form some 8 per cent., while 'Malays' (who are mostly in fact Javanese and Boyanese) another 9 per cent. The remaining 3 per cent. consists of Europeans, Eurasians, Jews, etc. The industries were mainly concerned with the handling of tin and rubber and pine-apples for export. There were some factories for local consumer goods. The 'Straits born' Chinese, some of the Malays and the Eurasians are the truly indigenous, and they only form a small proportion of the total population. The other inhabitants are mostly male, mostly between 25 and 50 years of age, and mostly come to Malaya to find work. If they can they will return to China, to India or to Europe when they are old, with or without a fortune.

Social services. There were several well-equipped modern hospitals. The Chinese, Indians and Eurasians came to hospital fairly readily, but the Malays were conservative and were rarely willing to accept western methods, although they were the only members of the population who received free education.

The General Hospital had two wards accommodating 120 children under six years old. They admitted about 3000 cases per annum, and the teaching on paediatrics was done in these wards. The mortality amounted to nearly 50 per cent. of admissions, as the babies were very frequently brought in moribund—merely to avoid funeral expenses in a poor household. It is hard to break a vicious circle; on account of the large proportion of deaths many people were unwilling to have their children admitted. Unfortunately the wards were not associated with the out-patient department, nor with a system of home visiting, and therefore any sort of follow-up work was difficult. The municipal welfare service was only extended to babies under one year of age, though with the rural welfare service it was possible to obtain excellent co-operation. On the whole, therefore, paediatric experience was overweighted with moribund medication and morbid anatomy.

Economic background. Most of the children come from the poorer classes. The father is a coolie getting 10 to 20 dollars per month. (One Straits Settlements dollar equals two shillings and

fourpence.) He lives with a wife and a few children in a cubicle 8 by 10 feet, for which they pay 3 to 5 dollars per month. The father has periods of unemployment or he may have expensive habits, such as opium smoking and gambling. The mother has to make something extra by working as a coolie, in a factory, by domestic help, or as a hawker. The children are left in charge of some indigent old woman, or else left locked up in the cubicle while the parents are out. The baby is hung up in a sarong from the roof. The younger children may scarcely ever go outside. The cubicle may be on the second or third floor—one of eight running from back to front of the house. Only the cubicles at the two ends of the row have any windows. It is reached by flights of narrow stairs. Perhaps as many as thirty other families live in the house. On the ground floor is the only latrine, of the bucket variety. The only cooking place is next door to it. The only water supply is a tap on the ground floor.

Rice is the staple diet, generally polished rice, and some salted vegetables imported from China, with, occasionally, dried fish and a little pork. Greens are eaten whenever possible. Old people go through the rubbish bins and pick out the discarded cabbage leaves. They tear out the bruised portions, and sell what they have salvaged at one cent. a handful. Unpolished rice can be bought, but the cheap varieties are full of broken and unhusked grains, so that it gives rise to enteritis unless it is picked over. It takes longer to cook than the polished, so that it costs more in fuel and time spent than the polished variety. Cooked food is often bought because of the saving of time, fuel and trouble. If the mother is ill or pregnant, even the small children are given a few cents to buy food from hawkers or at the numerous chop-houses.

Children are usually treated with affection, but the practical expression of affection is strictly limited by economic considerations, and by profound ignorance of hygiene. Babies are a luxury—highly valued if you can afford them. Babies that are unwanted may be sold or given away or abandoned. In spite of the large excess of males over females among the immigrant population (about 100 to 70) girls are still regarded as undesirable. In one year 575 unwanted babies were left at the Convent of the Sacred Heart. Of these only thirteen survived.

Nutrition of children. Beri-beri and tuberculosis are rampant. Malnutrition exists in every degree and in nearly every form. Nearly all cases admitted to the wards are due to, or complicated by, some sort of malnutrition, whether it be due to faults in the choice, in the preparation, or in the consumption of food.

Some cases of malnutrition are dramatic and well defined, while many are vague and subclinical. The diseases due to food deficiencies are of comparatively recent interest, and much remains yet to be known about the vitamins and the conditions resulting from the lack of them. It is a mistake to think that the natives of a country are those who know how to make the best use of its resources. Malays and Chinese, Tamils and Eurasians, and Europeans as well, all have their misguided and disastrous ideas about food and about the care of children. As the majority of the Singapore population is Chinese, it is to them chiefly that these remarks apply.

Considering the wealth of the place, the absence of epidemics, the healthy climate and good water supply, the infant mortality is excessive.

INFANT MORTALITY RATES

	1937	1938	1939	1940
England	58	53	50	55
Singapore, rural area ..	103	104	68	92
Singapore, municipal area	171	177	147	160

It is probable that this excessive infant mortality rate is due to malnutrition more than to any other factor, as the mortality rate for children of over one year is not high. Malnutrition results from ignorance and poverty, and the particular ways in which these factors manifest themselves are in artificial feeding, including improper substitutes for breast milk, in bad housing conditions and in wrong methods of child management.

Artificial feeding and social customs. Although the Indians as a whole are poorer than the Chinese, they have the smallest infantile mortality rate. They are the only race that adopts breast feeding as a matter of course.

INFANT MORTALITY RATES BY RACE

	CHINESE	MALAYS	INDIANS	AVERAGE ALL RACES
1937	172·9	229·8	139·5	171
1938	179·0	235·0	129·0	177
1939	150·3	188·0	96·9	147

Artificial feeding is a serious problem among the wealthy Chinese. Among the poorer classes it is a fearful scourge. The wealthy Chinese often give out their babies to a foster-mother to wet or dry nurse. The educated and semi-educated give all manner of excuses for not breast feeding the baby. The following are some of the reasons for artificial feeding:

(1) The Chinese despise the normal female figure, and the women wear tight bodices which produce atrophy of the breasts and depressed nipples. This is, racially, far more damaging than the custom of binding the feet. It is remarkable that it has received so little notice from their national leaders.

(2) The mother has to go to work and the baby is left at home in charge of some other child or some old woman.

(3) The mother is sick and cannot feed the baby. Malnutrition, especially that leading to beri-beri, is exceedingly common and has an adverse effect on lactation.

(4) The grandmother, or the senior wife, or some other relative wishes to take control of the baby.

(5) The people are poor, and the baby is sold to someone else, or given away to a relative who is

better off or who has fewer children. If the baby is sold, the transaction must take place through a recognized 'go-between.' The price varies very much. It may be over 300 dollars for a healthy little boy, whereas a sickly girl might be given away with a dollar or two to boot. There are some people who definitely gamble in children. They will go to the mother of a sick child and say, 'This baby isn't much good. It will probably die. I'll give you a dollar for it.' The child is sold, and often it is brought to the hospital. If it dies, the dollar is gone, but if it recovers, then it is sold again at a much higher price. One baby we admitted had been exchanged for 6½ lb. of rice, mee and pig's trotters. Frequently a girl is bought or adopted as the prospective wife for a boy in the family, or as a 'Mui Tsai.' It is hard to understand why these 'little sisters' have been so singled out for attention by reformers. As a matter of fact they only form a small detail in a complicated and often distressing social picture. But the distressing features arise from generalized ignorance, poverty, dirt and exploitation, not from the custom of adopting Mui Tsai. It is fashionable among wealthy Malays to buy a little Chinese girl. They are brought up as household attendants, and marry into the Malay families. They are thus acquiring merit by bringing unbelievers into Islam, and 'whitening up' the family complexions.

(6) With the existing reluctance of the Chinese to breast-feed their babies there is the natural corollary of poor technique in the management. It is remarkable to see how unwise and how unhandy a Chinese woman may be in matters pertaining to mothercraft. This applies to every class, from the towkays to the coolies. Added to the poor technique there is the misguided popularity of sweetened condensed milk. The palatable sweetness of this, when it is once started as a supplementary or as a complementary feed, often results in the baby refusing to take the breast, or taking the breast with no enthusiasm and finally in the drying up of the milk. With wearisome and deadly frequency one hears 'the baby would not suck,' 'the breast milk disappeared in three weeks,' and in every case it is proved that sweetened condensed milk had been given.

(7) The advertisements of the milk firms are responsible for a certain amount of misguided propaganda. The people they employ are not always wise in their methods and it may be found that artificial feeding and infant mortality are higher in those areas where milk firms have their 'nurses' working than in those where they do not.

(8) Among the school-teacher and shopkeeper class, where the mother is a worker, artificial feeding for the infant will enable her to continue with her occupation. The mother's understanding of child management is exceedingly imperfect owing to the defects of our educational system. In the Government service women are only given two to six weeks leave after confinement, so they cannot breast-feed their babies and retain their posts. This regulation has done much to encourage artificial feeding and to damage child life.

Method of artificial feeding. The above eight clauses are the most important in explaining the prevalence of artificial feeding. We should now examine why it is so particularly harmful.

(1) The sanitary standards of the population are low. Housing conditions are often bad, and the almost universal prevalence of the round worm is some indication of the unhygienic habits. Cases of ascariasis have been found as young as three months of age. Most households are incapable of preparing a baby's feed in even a remotely sanitary manner.

(2) The wages earned by the average household make it difficult or impossible for them to buy tinned milk in sufficient quantities to feed the baby adequately. The result is that the sweetened condensed milk is often diluted to one in thirty (instead of one in six or eight). It is often mixed with rice or wheat or cornflour, which may or may not be properly cooked before it is given.

(3) If the baby is not fed by the mother he is often left to the care of someone less capable of looking after him.

(4) If sweetened condensed milk is used for infant feeding over a long period, the baby needs plenty of sunshine and additional supplies of vitamins, especially of the fat-soluble vitamins. There is only a very small percentage of the population in Singapore who attend welfare centres or orthodox doctors regularly, and few indeed that receive cod liver oil as part of their diet.

SWEETENED CONDENSED MILK. The artificial feed that is by far the most widely used is sweetened condensed milk. It is well known that this can be a most useful infant food, but that if continued as the only food over a long period it tends to make the child fat and flabby, subject to boils, to diarrhoea and catarrhs and to rickets. Happily the only sweetened condensed milk that is permitted for sale by the Government is the full cream variety. But this is often diluted so much that it is a poor diet. Even the orthodox mixture of one in six or one in eight is very poor in fat.

	CALORIES IN ONE OUNCE	FAT (per cent.)	PROTEIN (per cent.)	CARBOHYDRATE (per cent.)
Full cream sweetened condensed milk	102	9·0	8·7	53·0
Sweetened condensed milk, one in eight ..	13	1·1	1·1	6·5
Human milk ..	20	3·5	1·2	6·5

The poor fat content is not the only disadvantage of this mixture. There is also a shortage of the fat-soluble vitamins. Different brands of tinned milk are sold at widely different prices, although they all give approximately the same analysis. Generally speaking the more expensive brands were those prepared from meadow-fed English cows in the summer and from meadow-fed Australian cows in

the antipodean summer. The cheaper brands came from stall-fed cows, generally Dutch and Danish. Professor Rosedale kindly estimated the Vitamin A content of the cheaper brands and the figures for vitamin A proved to be extremely small. This investigation was undertaken after it had been noted that of thirty consecutive admissions of babies blind or partially blind from keratomalacia, 28 had been fed on sweetened condensed milk. It will be seen that rickets also is prevalent among babies fed on this milk.

Etiology and diagnosis of rickets. Rickets is produced by two major and is associated with two minor factors. The major factors are (1) improper feeding, and (2) insufficient sunlight. The minor factors are (1) prematurity, and (2) congenital syphilis.

Both the minor factors are easy to eliminate. Prematurity can generally be excluded by reference to the history (and the welfare card), and congenital syphilis by blood tests on the baby and its parents and by x-ray appearances. It has been found that these minor factors are only associated with a very small proportion of the cases of rickets.

When considering the diagnosis and the importance of rickets in this place there are various points to bear in mind :

Rickets is primarily a disease of growth. Where malnutrition leads to defective growth, then rickets is only seen in minor degree. In many of the babies with whom we were dealing the total quantity of nourishment received was so very small that the degree of rickets was comparatively inconspicuous. Malnutrition may be so severe that at two and three years old the child only weighs 12 to 14 lb. These are not the children one sees running about in the streets, and children over one year are not visited by the Municipal Health Nurses, so that it is only when they are brought to the hospital (and that is often only when they are moribund) that the disease is seen. Minor degrees of rickets in an ill-nourished child are just as significant as florid rickets in a well-grown child.

The popular diet is poor in calcium. The early osseous changes in rickets result from an absence of lime salts in the more recently formed parts of the bony skeleton. These do not necessarily (per se) harm the child. But even mild degrees of bony changes may be accompanied by a serious predisposition towards catarrhal conditions of respiratory and digestive tracts. These are the results of rickets that endanger life.

Conditions which lead to the appearance of rickets, and the anaemia which invariably accompanies rickets, are those conditions which result in a high rate of infantile mortality and morbidity.

The presence of rickets is generally proved by x-ray appearances. It must be remembered that there are many early cases in which, if a post mortem is done, rickets can be recognized in histological sections, whilst the condition is as yet too early to show radiographical changes.

There are many children who show slight beading of ribs and early radiological changes in whom there is no evidence of illness or of any general disturbance. These cases are common among a well-cared-for population. But in the stress and strain of slum life in Singapore it appears that very mild signs of rickets may be associated with catarrhal conditions which prove fatal.

The subject of rickets has not in the past been brought to the attention of the medical authorities in the locality. Although cases were constantly treated in the hospital from among babies attending welfare centres in the town, it was not a disease that was ever diagnosed by the staff of these centres, and there were many doctors who disputed the existence of the condition. It had, however, been recognized by Matron Simmons in the rural areas.

In this paper cases are only classified as rickets if the diagnosis was confirmed, either by x-ray or by post-mortem appearances. In addition to these there were numerous cases, especially among those that died very shortly after admission and before they could be investigated, in which signs of rickets were forgotten or unidentified behind a fulminating secondary condition, such as enteritis, meningitis and pneumonia, so that the real incidence of the disease is probably larger than that shown in the figures given in the appendix.

Age of incidence. In wards for children up to six years of age it was found that most of the cases of rickets were in children who were between three and sixteen months of age. It was not uncommon as early as six weeks. This is early compared with the age of incidence in other countries.

It is rare to see cases of genu valgum or contracted pelvis or any evidence of rickets in the adult population. This is because the disease is limited by the social and domestic conditions already described. The babies and children often live inside dark stuffy cubicles. If they get rickets they may die from some intercurrent disease. If they survive the first year or two of life, then they go outside and the progress of the disease is automatically arrested by the strong sunlight.

Race. The majority of the cases we saw were among artificially fed Chinese babies. Chinese formed about 90 per cent. of the children in the wards. Among the small number of Indians admitted to the wards, nearly all were breast fed. Some very severe cases of rickets were met in breast-fed Indian babies. These were mostly among the Sikhs, who live a semi-purdah life. It is recognized that the pigmentation of the skin favours the development of rickets if the other factors are present.

Clinical picture. BEADED RIBS. This was found to be the earliest and most reliable sign. Any baby that on palpation showed signs of irregularity along the costo-chondral junction was investigated for rickets. In fat babies it was impossible to see, and often difficult to feel, this beading. Marked beading was invariably accompanied by advanced radiological changes.

ENLARGEMENT OF EPIPHYSES. This is generally noticeable at wrists and ankles.

CRANIOTABES. Park and Eliot (1933) state that craniotabes is often the first definite sign of rickets. This observation in Baltimore has not been confirmed in Singapore. No single case of craniotabes has been met with, although it has been faithfully sought for in every child.

BOSSING OF THE HEAD. Few well-marked cases are seen, possibly explained by the unusually early incidence of the disease.

DEFORMITIES OF THE LIMBS. These are also rare in any marked degree, but this is only to be expected as the story-book deformities do not generally appear until the limbs begin to bear the weight.

ATONICITY OF MUSCLES AND LAXITY OF LIGAMENTS. These are often well marked. They produce ' the belly of the poisoned pup,' marked kyphosis, lateness in walking and genu recurvatum. Generally, flaccidity is increased by the other dietetic defects, such as beri-beri and underfeeding.

SWEATING OF THE HEAD is not conspicuous as a symptom. Sweating, sudamina, and septic skin conditions are excessively common in any case.

ANAEMIA. The average haemoglobin for children in Singapore is well below the ' normal ' in London. But in cases with rickets it was generally found that the anaemia was more conspicuous—even profound. It was of the usual secondary type.

DENTAL CARIES. The Chinese, as a rule, have very bad teeth. Ricketty Chinese children showed the delayed dentition and dental caries that are typical of rickets. But among the Indian children, who were incidentally nearly always breast fed, it was found that even a case of ' gross rickets ' might have a perfect set of teeth.

SPLENOMEGALY. This was generally slight and often absent.

SECONDARY INFECTIONS. As our cases were limited to those admitted to hospital it was not possible to estimate the number of children among the general population who showed signs of rickets without other symptoms. But it appeared from our purely institutional experience that those who showed x-ray evidence of rickets were subject to high morbidity and mortality from gastritis, enteritis, convulsions, otitis, meningitis, septic skin conditions and respiratory disturbances.

CONVULSIONS. These are very frequent and will be referred to under ' Rickets with tetany.'

Pathology. Biochemical examination was not always possible owing to the condition of the patients and also to the shortage of staff.

PLASMA PHOSPHATASE is usually considered the most accurate indication of the degree of rickets. Unfortunately for lack of the necessary reagents we were unable to carry out this estimation.

BLOOD CALCIUM. Normally this is 10 to 12 mgm. per cent. In rickets it may be normal, but in ' low calcium ' rickets it may be reduced to as little as 4 per cent. and these cases are often accompanied by signs of tetany and cerebral irritation. This is typical of the findings in Singapore.

SERUM PHOSPHORUS. This is usually 5 mgm. per cent. and in rickets may be reduced to 3 to 3·7 per cent. This was also mainly confirmed.

CALCIUM PHOSPHORUS MULTIPLE. It has been said that Ca × P should be 40 or over. It was found in practice that many a child with a multiple of well over 40 still suffered from undoubted rickets.

Radiology. The radiological changes were in no way different from those generally seen. The presence of subperiosteal osteoid tissue was often a prominent feature, and sometimes appeared before the other bony changes. At first some difficulty was experienced in persuading other doctors that this feature (i.e. described as periostitis in the X-ray reports) was not necessarily a sign of congenital syphilis. In fact there is usually a considerable difference between the coarse, irregular periostitis of syphilis and the regular, delicate, symmetrical ' subperiosteal osteoid ' of rickets. The former is also usually accompanied by irregular thickening of the bones, which is not present in rickets.

Malnutrition is exceedingly common, and besides predisposing towards deficiency diseases, of which beri-beri is by far the commonest and rickets the next, the diet is conspicuously poor in calcium. A great many x-rays, besides those that show rickets, show bones that are poorly calcified. The poverty in calcium, probably in combination with other deficiencies, appears to alter the maturation of the bones, producing some premature ossification. It has been observed that the ' radiological age ' of young girls is often two or three years in advance of the age given on their birth certificates. It is inviting to postulate a theory that the anaemia which is always found in rickets, and which is so terribly common and intractable in many Asiatics, may be associated with faulty development, not only of the calcified parts of the bone, but also of the blood-forming organs of the marrow.

Morbid anatomy. We were able to obtain a large number of post mortems, and to confirm the usual findings, both gross and microscopic. Many cases showed histological evidence of rickets, appearing first at the costo-chondral junction, where there was only slight beading present, while the x-ray appearance was still negative: e.g. Case No. 2353/40 (1940 series).

This was a Chinese female infant of two months old, fed from birth on sweetened condensed milk. The infant was admitted with fits. There was beading of the ribs and both Ca and P were low (8·5 and 3·7). The x-ray showed little evidence of rickets, but after the post mortem, sections of the costo-chondral junctions showed rachitic changes, which were absent in the femur.

The periostitis of congenital syphilis showed round-celled infiltration which distinguished it from that of rickets.

Types of rickets. RICKETS WITH TETANY. Cases with fits were often associated with a low blood calcium, e.g. table 2, cases 1647, 1898, 1987, 2004, 2021, 2083, 2196, 2345, 2353, and 2359.

'Infantile convulsions' is given as a cause of death in a very large number of babies in the Singapore statistics—especially in cases which have not attended the hospital and therefore are unlikely to be accurately diagnosed. It is probable that a large proportion of these fatal cases of convulsions are associated with tetany, with or without rickets

Convulsions are exceedingly common in babies, and calcium deficiency is an important one of the many causes. Subacute cases of beri-beri are often associated with convulsions and head retraction (cf. the experimental pigeon rather than with beri-beri in adults). Nutritional disturbances, helminthiasis, particularly ascariasis, and meningitis are all excessively common. Calcium deficiency and tetany are not yet sufficiently widely recognized as a cause of convulsions and often even if it is suspected, the calcium given in treatment is not sufficient to correct the deficiency, e.g. Case 2644 (1940 series):

Chinese male, aged three months. Breast fed one week, then given sweetened condensed milk; admitted to another ward with severe convulsions. Was treated with intramuscular calcium gluconate solution 10 per cent. 2 c.cm. daily. The cerebrospinal fluid was found to be normal. The fits persisted and three days later the infant was transferred to the writer's wards with a diagnosis of 'encephalitis.' The convulsions were still persistent and violent. The blood calcium was then estimated and proved to be 5 mgm. per 100 c.cm. and the phosphorus 6·5 per 100 c.cm. The calcium gluconate solution was increased to 10 c.cm. twice daily and was accompanied by adexolin and calcium by mouth. At once the child improved and was discharged fit in a short while.

RICKETS IN PREMATURE BABIES. This type of rickets was severe and obstinate and apparently could not be prevented by any means at present at our disposal. Premature babies, if they were kept inside the ward, invariably became rickety, and even if they were nursed systematically on the balcony, they still developed a mild degree of osseous rickets, although the secondary catarrhs might be comparatively mild or absent. The climate is warm throughout the year so that they had little or no covering, and were only brought inside on account of rain. It appeared that Indians, with skins more deeply pigmented, were more prone to this type of rickets than the Chinese, e.g. Case No. 1769 (1940 series):

Chinese female, aged six months. Birth weight 2 lb. 6 oz. Had been breast fed and well cared for, and visited regularly by a health nurse, but had not been given any vitamin D. At six months the infant weighed 8½ lb. Beading of the ribs was well marked. X-ray report stated 'gross rickets.' The infant developed diarrhoea and pneumonia and died.

RICKETS WITH CONGENITAL SYPHILIS. The incidence of congenital syphilis in Malaya has been wildly overestimated. The statement that 'fifty per cent. of the babies suffer from syphilis' has actually been made by individuals who should be counted as responsible. In actual fact, less than 3 per cent. of the sick children admitted to our wards showed any evidence of syphilis. It is true that there is a great deal of venereal disease in the adult population, both in town and country areas. But it must be remembered that social and economic conditions have produced a section of the population that is predominantly male, that comes to this country in order to make money and then return home to another country. This is the population which does not breed, but in whom syphilis is rampant. The other section of the population that settles down and makes its home here, and which does breed, has relatively little venereal disease. At Tan Tock Seng, the large male hospital, in taking histories one often gets the reply 'No, I have not got venereal disease, I am a married man.' (This is another illustration of the desirability of cultivating a 'Straits born' population, rather than tolerating the large infant mortality and then depending on labour that has to be imported.)

Cases that have formerly been called syphilitic are mostly nutritional deficiencies and marasmus. In rural areas where yaws is prevalent the majority of the positive W.R. and Kahn tests are due to yaws and not to syphilis. Among 2000 admissions (table 1) there were nineteen cases of congenital syphilis, of which four were proved to have rickets as well. It would seem that the incidence of rickets among congenital syphilitics is high.

OBSTINATE RICKETS. Cases of rickets have been described which persisted in spite of every known form of treatment. These were not encountered in our experience with older children, but were only found among the premature babies. If no secondary infection intervened, then the cases as a whole responded rapidly, provided the treatment was adequate.

Case incidence. It will be obvious that owing to the impossibility of investigating all the cases that were admitted, it is equally impossible to give an accurate estimate of the incidence of a disease such as rickets. But by reference to the tables given it will be seen that of 2,000 admissions of children under six years old between January and September, 1939, there were 81 diagnosed as rickets, either by x-ray examination or post mortem findings. In a series of 1000 consecutive admissions in August to November, 1940, when investigations were more complete, 100 cases were found to have beaded ribs. Of these 83 were x-rayed and 59 of them showed radiological evidence of rickets.

Treatment. It is apparent that the rickets with which we are principally dealing is due to lack of vitamin D and lack of mineral salts. The majority of cases responded well to treatment, e.g. table 1. Admission No. 1543 on 26 June, 1939:

A Chinese male infant, aged eight months, had been fed from birth on sweetened condensed milk,

with occasional breast feeds for the first month. For one week the infant had had fever and cough.

The Wassermann reactions of the mother and father were negative; a brother, aged three years, was healthy; a sister had died at the age of six months.

On admission, the infant was cyanosed, flabby and dyspnoeic; the knee jerks were sluggish and the heart rapid. Examination of the chest showed moist sounds. The infant's weight was 12 lb., temperature 101° F., pulse ++. The respiration rate was 60. The ribs were beaded +++ and the joints enlarged. There was no craniotabes. X-ray diagnosis: Rickets ++ with 'periostitis' ++. W.R. negative, and after provocative dose of arsenicals remained still negative.

The diagnosis of pneumonia, beri-beri and rickets was made.

TREATMENT. The infant was given nasal oxygen and intramuscular vitamin B1, 2000 units daily for three days, and atropine. The condition of the chest and heart improved rapidly. Further treatment consisted of adexolin minims 10 t.d.s., Meads mineral tablets, 1 t.d.s., and ultra-violet light (ten treatments).

PROGRESS. 19th July, 1939. 'Well-marked improvement' (x-ray report).

9th August, 1939. 'Further satisfactory progress' (x-ray report).

The infant was discharged fit in two months.

NOTE. The rapid progress could be seen in the x-rays. The radiologist reported that the x-ray appearances were those of syphilis, but as a clinician I was unable to agree. This child had been visited seven times by the Health visitor, but the three-hourly feeds, the washing of the bottle, and the water in between feeds which was persistently recommended had done nothing to prevent either the beri-beri or the rickets.

It was noticed that the cases that were given calcium combined with other mineral salts seemed to recover more quickly than those that received calcium only.

A few cases were given large 'depot' doses of calciferol as recommended by some American authors, and, as far as our observation went, they also progressed favourably.

Among the premature babies we found that although we could not prevent rickets, yet with close attention to diet and regimen, the harmful secondary infections might be avoided. Anaemia in these babies was an obstinate symptom, sometimes needing transfusions.

Among congenital syphilitics it was found almost hopeless to treat either the rickets or the syphilis unless the babies were breast fed. It was possible to do a fair number of routine Kahn or Wassermann tests, both on the babies and on the parents, and it was very rare that clinical findings differed from serological, so that I cannot believe we were missing cases of congenital syphilis.

Cases that had convulsions often needed the most drastic treatment, and were often fatal in spite of it. Calcium had to be given in large doses and by every available route. Convulsions sometimes could only be controlled by frequent inhalations of chloroform. Lumbar puncture sometimes had to be performed three or four times a day and clear fluid under excessive pressure was removed on each occasion. In one child with a particularly large opening, the tense, bulging fontanelle looked like a small pyramid on the top of the head. Aperients and enemata were also used. Of the sedatives, chloral and bromide and sometimes luminal were given. Acidosis was also treated.

Prevention. In all paediatric subjects prevention is the most important aspect and rickets in this country is eminently preventible.

The first necessity is education—

(a) of the doctors, so that the disease receives some attention and adequate treatment;

(b) of the dressers and nurses and health visitors, so that they recognize the disease and can advise how it should be prevented;

(c) of the population, so that they learn how to provide the proper food and care and sunlight for the babies.

The other measures—improved housing and improved social conditions, so that mothers of young babies can stay at home and feed them instead of going out to work, will come with improved education.

I should like to record my gratitude to the sisters and nurses with whom I have worked, to my various House Physicians, particularly Dr. William Heng, M.B., D.C.H.; to the pathologists, particularly Dr. L. S. da Silva for studies of morbid anatomy and Dr. R. Sreenevasan for blood chemistry; to the radiologists for their patience with my cases and with my arguments; and, finally, to Mrs. MacCarthy and Mrs. Mackenzie who have done the typing, often under difficulties.

POSTSCRIPT. These figures and records were made between September, 1937, and February, 1941, during which time, apart from periods of leave, I was in charge of the children's wards at the General Hospital, Singapore, and Lecturer in Paediatrics at the College of Medicine. In early 1941 I went to the Unfederated State of Trengganu, in order to hold locum for the state medical officer, and to start welfare work. In December, 1941, we had to escape hurriedly through the jungle, carrying our own loads. The journey took ten days. The notes on rickets were at the bottom of my pack, but unfortunately not the histological slides. In Singapore I was in charge of the children's wards (then transferred to Tan Tok Seng Hospital) when we were forced to evacuate 120 children back to the General Hospital at twelve minutes' notice. I was permitted to visit the old quarters some weeks after the capitulation, and though the things had been looted, the notes on rickets were still lying on a shelf. They went with me into internment at Changi Prison, which afforded leisure to write them up. These observations are obviously very defective, but there has been no access to hospital records to complete them and little access to books of reference. For these and other defects, apologies are offered.

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APPENDIX

CHILDREN'S WARDS, GENERAL HOSPITAL, SINGAPORE, JANUARY TO SEPTEMBER, 1939

ANALYSIS OF 2000 CONSECUTIVE ADMISSIONS (children under 6 years)

Deaths—post mortem	228	
No post mortem	530	758
Not improved and transferred		198
Improved		600
Cured		288
Still in hospital		
Lodgers		156
Records incomplete		
Total		2000
Cases with clinical evidence of rickets		118
Rickets diagnosed by x-ray or post-mortem evidence		81
Total cases of congenital syphilis		19
Congenital syphilis plus rickets		4

Cases 304, 640, 1257 and 1347 were reported on by the radiologist who, at that time, believed that what he described as periostitis was invariably associated with congenital syphilis; therefore the diagnosis may be considered in doubt, and the cases should probably be classified among the 'rickets.'

Histories of feeding, etc., are often incomplete if the patients were admitted at night, or the relatives did not appear again, or could not be traced.

Abbreviations used in tables.

Race—C=Chinese, I=Indian, M=Malay.
N.I.=Not improved and transferred.
P.M.=Died and post mortem.
S.C.M.=Sweetened condensed milk.

TABLE I

INCIDENCE OF RICKETS AMONG 2000 CONSECUTIVE ADMISSIONS, JANUARY TO SEPTEMBER, 1939

(Rickets and some other conditions are described.)

Case No.	Age (months)	Race	Sex	Result	Notes	Diagnosis
20	3	C	F	Died	Old case of rickets and anaemia—admitted with pneumonia. Had been fed on sweetened condensed milk.	Rickets and pneumonia.
40	5	C	M	Improved	Fed on S.C.M. X-ray 'suggestive rickets.' W.R. and Kahn negative.	Rickets.
41	2	C	M	Improved	Fed on S.C.M. X-ray 'suggestive of minor rachitic changes.' W.R. and Kahn test negative.	Rickets and anaemia.
	2	C	M	P.M.	Artificial feeding. X-ray 'slight but definite rickets.	Rickets and enteritis.
51	4	C	M	Improved	S.C.M. X-ray 'slight rachitic changes.'	Rickets.
57	2	C	M	Improved	S.C.M. X-ray 'definite but not marked rickets.' Haemoglobin 50 per cent.	Rickets and anaemia.
62	7	C	F	P.M.	X-ray 'slight but definite rickets.'	Rickets, beri-beri and pneumonia.
74	2	I	M	N.I.	S.C.M. X-ray 'definite rickets.'	Rickets.
76	2	C	M	Improved	S.C.M. X-ray 'minor rachitic changes.'	Rickets.
103	2	C	M	P.M.	Ribs beaded, etc.	Rickets.
115	6	C	M	Improved	Ribs beaded.	Malnutrition.
122	4	C	M	P.M.	Ribs beaded. Head retraction and engorgement of brain due to ? beri-beri, ? calcium deficiency.	Meningismus.
188	3	C	M	Improved	S.C.M. since birth. Beaded ribs.	Malnutrition.
202	7	C	M	Improved	S.C.M. Ribs beaded. X-ray negative.	Malnutrition.
219	6	C	M	P.M.	Breast fed 3 months, then S.C.M. Admitted with severe convulsions, not controlled by vitamin B or by calcium. W.R. negative. X-ray 'rickets.'	Rickets.
304	3	C	F	Improved	Furunculosis. Beaded ribs. X-ray 'periostitis.' W.R. negative.	Furunculosis.
326	2	C	F	Improved	X-ray 'minor rickets.'	Rickets.
327	2	C	M	Improved	S.C.M. W.R. negative. X-ray 'suggestive rickets.'	Rickets and beri-beri.

TABLE 1.—*continued*

Case No.	Age (months)	Race	Sex	Result	Notes	Diagnosis
339	3	C	F	Improved	S.C.M. X-ray ' definite rickets.'	Rickets and beri-beri.
342	5	C	M	N.I.	S.C.M. Beaded ribs. No x-ray.	Malnutrition and diphtheria.
354	4	C	M	Improved	Congenital syphilis—Kahn test positive.	Congenital syphilis.
377	2	C	M	P.M.		Rickets and enteritis.
386	6	C	F	Improved	S.C.M. X-ray ' minor rickets.'	Rickets.
394	4	C	M	Improved	S.C.M. (adopted child). X-ray ' definite rickets.'	Rickets.
427	2	C	M	Improved	Breast fed. Anaemic. Beaded ribs. X-ray negative.	Anaemia.
430	10	C	F	Improved	Mixed feeding. S.C.M. and breast milk. X-ray ' rickets present.'	Rickets.
439	1	C	M	Improved	Breast fed. Ribs beaded. Convulsions. X-ray negative.	Convulsions.
460	2	C	M	Died		Congenital syphilis.
463	4	C	F	Improved	S.C.M. X-ray positive.	Rickets.
478	4	C	F	Improved	S.C.M. X-ray ' suggestive rickets.'	Malnutrition and rickets.
493	2	C	F	Improved	Mixed feeding. X-ray ' definite rickets.'	Rickets.
500	3	C	M	Improved	Mongol. W.R. negative. X-ray ' rickets present.'	Mongolism and rickets.
512	3	C	M	Improved	S.C.M. W.R. negative. X-ray ' marked rickets.'	Rickets.
515	13	C	F	Cured	S.C.M. X-ray ' healing rickets.'	Pyelitis and rickets.
522	7	C	M	Cured	Beaded ribs. X-ray negative.	Pyelitis.
533	3	C	F	N.I.	X-ray ' slight periostitis.' W.R. positive.	Congenital syphilis.
565	7	C	M	P.M.	Old case readmitted with pneumonia.	Rickets and pneumonia.
599	3	C	M	Died		Congenital syphilis.
607	5	C	F	Improved	Old case readmitted.	Rickets and bronchitis.
640	3	M	F	Improved	S.C.M. Beaded ribs. X-ray ' periostitis.' W.R. negative.	Enteritis and ' periostitis.'
644	8	C	F	Died	Well-marked beading, etc. Bronchitis and beri-beri.	Rickets and bronchitis.
673	3	C	M	N.I.	S.C.M. X-ray ' definite rickets.'	Rickets and enteritis.
686	10	C	M	N.I.	X-ray ' doubtful syphilis.' W.R. negative.	Epiphysitis and enteritis.
735	1	C	M	Improved	Beaded ribs. X-ray negative.	Pneumonia.
738	3	I	F	Improved	S.C.M. Beaded ribs. X-ray negative.	Malnutrition.
777	5	C	M	Cured	Old case of rickets. Beri-beri and pneumonia.	Beri-beri and pneumonia.
824	4	C	M	Improved	S.C.M. X-ray ' definite rickets.'	Rickets and convulsions.
876	2	I	F	Died	S.C.M. ' Born with deformities.' X-ray ' marked rickets.'	Rickets.
887	9	C	M	Improved	Beaded ribs. X-ray negative.	Whooping-cough and enteritis.
892	17	I	F	Improved	X-ray ' marked rickets.'	Rickets, ascariasis and pneumonia.
897	10	C	F	N.I.	S.C.M. X-ray ' suggestive rickets.' Beaded ribs.	Rickets and enteritis.
918	6	C	F	Improved	S.C.M. Beaded ribs. X-ray ' marked rickets.'	Rickets.
936	2	C	M	Improved	Breast-fed. Some beading. W.R. +++. X-ray ' rickets and periostitis.'	Congenital syphilis and rickets.
964	8	C	F	Improved	S.C.M. Beading of ribs ++ X-ray negative.	Enteritis.
965	4	C	M	Improved	S.C.M. Beading + X-ray ' well marked rickets and periostitis.' W.R. negative.	Rickets and enteritis.
975	2	C	F	Improved	S.C.M. Beaded ribs. X-ray ' minor rickets.'	Rickets and enteritis.
991	2	C	M	Died	S.C.M. Syphilis. Kahn test +++ X-ray ' periostitis and defective occification.'	Congenital syphilis.
1002	7	C	F	Died	Enteritis, etc. Beaded ribs. X-ray ' rickets, marked.'	Rickets.
1004	2	C	M	N.I.	Beaded ribs. Anaemia +. X-ray ' marked rickets.'	Rickets and anaemia
1007	24	C	M	Died	S.C.M. Ribs beaded. X-ray ' bones poorly calcified.'	Malnutrition.
1010	36	C	M	Improved	Beaded ribs. X-ray ' no rickets.'	Malnutrition and pneumonia.
1012	12	C	M	N.I.	S.C.M. Anaemic. Beaded ribs. X-ray ' early rickets.'	Rickets and anaemia.

TABLE 1.—*continued*

Case No.	Age (months)	Race	Sex	Result	Notes	Diagnosis
1022	3	C	F	Died	Old case of rickets. Convulsions ++.	Rickets and convulsions.
1033	4	C	F	P.M.	S.C.M. X-ray 'rickets present.' Cerebral irritation.	Malaria and rickets.
1041	2	C	F	Improved	S.C.M. X-ray 'minor rachitic changes.'	Rickets and convulsions.
1046	7	C	M	Improved	Breast fed. X-ray 'healing rickets.'	Rickets and convulsions.
1053	12	C	F	N.I.	Beaded ribs. Bronchitis. X-ray negative.	Beri-beri and bronchitis.
1054	7	C	M	N.I.	S.C.M. Beaded ribs. X-ray 'periostitis present—no rickets.'	Furunculosis and 'periostitis.'
1061	24	C	F	Improved	S.C.M. Appearance rickety. Weight 13½ lb. at 2 years. X-ray negative for rickets.	Malnutrition and bronchitis.
1063	6	C	F	Died	S.C.M. Beaded ribs. X-ray 'negative for rickets. Periostitis present.'	Malnutrition.
1077	5	C	F	Improved	S.C.M. Ribs beaded. X-ray negative.	Pyelo-nephritis.
1086	8	C	M	N.I.		Mongolism and rickets.
1090	6	C	M	Improved	S.C.M. Enteritis. Beaded ribs. Not x-rayed.	Enteritis.
1108	5	C	M	P.M.	Beaded ribs. X-ray 'rickets marked and symmetrical periostitis.' W.R. negative.	Rickets.
1137	7	C	M	Cured	Mixed feeding. Beaded ribs. X-ray negative.	Enteritis.
1142	1	C	F	Died	S.C.M.? Beaded ribs. X-ray 'minor rickets.'	Rickets and enteritis.
1170	2	C	M	Died	S.C.M. X-ray 'periostitis and cuffing.' W.R. and Kahn test negative.	Rickets.
1174	1	C	M	Died	S.C.M. Beaded ribs, etc. X-ray 'minor rickets and periostitis.'	Rickets and enteritis.
1177	3	C	M	Improved	S.C.M. Beaded ribs. X-ray negative.	Beri-beri.
1178	4	C	M	Improved	S.C.M. Beaded ribs. X-ray 'minor rickets and periostitis.'	Rickets and beri-beri.
1190	6	C	F	Improved	S.C.M. X-ray 'flaring and cuffing and erosion of cortex.' Kahn test negative.	Rickets and bronchitis.
1198	24	C	F	Improved	Syphilitic. W.R. +++	Congenital syphilis.
1201	4	I	M	Cured	Breast fed. Beaded ribs. X-ray 'minor rickets.'	Rickets.
1214	6	C	M	Improved	S.C.M. X-ray 'marked rickets.' Hb 29 per cent.	Rickets and anaemia.
1222	8	I	M	Improved	Breast fed. X-ray 'gross rickets and symmetrical periostitis.' W.R. negative. Both parents W.R. negative.	Rickets and convulsions.
1229	3	C	F	Improved	S.C.M. Beaded ribs. X-ray negative.	Beri-beri.
1257	3	C	F	Died	Beaded ribs. X-ray 'rickets and syphilis.'	Rickets and enteritis.
1288	4	C	M	Improved	S.C.M. Beaded ribs ++ X-ray negative.	Malnutrition.
1296	4	C	M	N.I.	Beaded ribs. X-ray 'rickets present.'	Rickets and pneumonia.
1297	1	C	M	Died	Beaded ribs ++ S.C.M.	Beri-beri and rickets.
1300	5	C	M	Died	Congenital syphilis and beaded ribs.	Congenital syphilis.
1304	1	C	M	P.M.	Emaciated. Beaded ribs. X-ray 'suggestive rickets.' Kahn test negative.	Beri-beri and rickets.
1347	8	C	M	Improved	S.C.M. Beaded ribs, etc. X-ray 'rickets and syphilis.' W.R. negative. Both parents W.R. negative.	Rickets and beri-beri.
1350	8	C	F	Improved	X-ray 'density of metaphysis.' Haemorrhages from gums, etc.	Scurvy.
1370	9	C	F	Died	Emaciated ++ Ulcers ++ Beaded ribs ++ X-ray for rickets negative.	Malnutrition.
1393	9	C	F	Died	Convulsions. Beaded ribs ++	Rickets.
1408	9	C	M	Improved	Old case re-admitted.	Rickets and ber-beri.
1420	8	C	F	Died	S.C.M. Beaded ribs. Syphilitic facies. X-ray 'periostitis.' Kahn test + Both parents Kahn test +	Congenital syphilis.
1460	¾	M	F	N.I.	Beaded ribs. X-ray negative.	Pneumonia and opthalmia.
1998	2	C	M	Died	Beaded ribs. Emaciated.	Malnutrition. Cellulitis.
1543	8	C	M	Improved	Beaded ribs. X-ray 'rickets and periostitis.' Kahn test negative.	Rickets and beri-beri.
1591	1½	C	M	Improved	Breast fed. Beaded ribs. X-ray 'slight flaring of ulna.'	Beri-beri and rickets.

TABLE 1.—*continued*

Case No.	Age (months)	Race	Sex	Result	Notes	Diagnosis
1600	1	C	F	Died	S.C.M. Anaemia, fits, enteritis. X-ray 'bands of increased density at epiphyses. Slight flaring of metaphyseal ends. No. periostitis.'	Rickets.
1601	¼	C	M	Died		Congenital syphilis.
1616	3	C	M	P.M.	S.C.M. X-ray 'periostitis and flaring of ulna.' Kahn test negative. Both parents Kahn test negative.	Rickets.
1625	1½	C	F	Died	S.C.M. Beri-beri. Beaded ribs. X-ray 'slight flaring of ulna.'	Beri-beri and rickets.
1666	6	C	M	Improved	Beaded ribs. Convulsions. X-ray 'rickets present.'	Rickets and convulsions.
1667	3	C	M	Improved	Beaded ribs. Convulsions. X-ray 'marked rickets.'	Rickets and convulsions.
1673	9	C	M	Died	S.C.M. Beaded ribs.	Rickets and pneumonia.
1677	2	C	F	Improved		Congenital syphilis.
1678	2	C	F	Died	S.C.M. Blind. X-ray 'rickets and periostitis.'	Rickets and keratomalacia.
1693	7	C	F	Died	X-ray 'rickets and periostitis.' W.R. negative.	Rickets.
1698	16	C	M	Improved	Beaded ribs and laxity of ligaments. X-ray negative.	Malnutrition.
1707	6	C	F	Died	S.C.M. Congenital heart. X-ray 'marked rickets.'	Rickets and con. heart.
1744	2	C	F	N.I.	Kahn test negative. W. R. +	Congenital syphilis.
1746	1½	C	M	P.M.	S.C.M. Convulsions. Kahn test negative. X-ray 'rickets present.'	Rickets and pneumonia.
1752	2	C	F	N.I.	S.C.M. Beaded ribs. Kahn test negative. X-ray 'dense line of arrested growth.'	Malnutrition.
1760	6	C	F	Cured	S.C.M. Beaded ribs. X-ray 'dense line of arrested growth.'	Beri-beri and pneumonia.
1769	2	I	F	Improved	Syphilitic. Beri-beri.	Congenital syphilis.
1775	6	C	M	Died	S.C.M. Beaded ribs. X-ray 'suggestion of periostitis and flaring.'	Rickets.
1832	12	C	M		Beaded ribs. Anaemia. X-ray 'rickets present.'	Rickets and anaemia.
1843	5	C	M	N.I.	Syphilitic. X-ray 'periostitis.' W.R. doubtful +	Congenital syphilis.
1852	2	I	M	N.I.	W.R. +	Congenital syphilis.
1859	3	C	F	Improved	Beaded ribs, etc. X-ray negative.	Malnutrition.
1883	¾	C	M	Died	W.R. + Kahn test +++	Congenital syphilis.
1942	6	C	F	Died	Beaded ribs. W.R. positive. X-ray 'positive for syphilis and rickets.'	Congenital syphilis and rickets.
1943	4	C	M	N.I.	Beaded ribs, etc. X-ray 'rickets present.'	Rickets.
1975	6	C	F	N.I.	Jaundice. Beaded ribs. W.R. negative. X-ray 'increased density of bone.'	Rickets and enteritis.
1988	4	C	M	Died	S.C.M. X-ray 'slight rickets, etc.'	Rickets and enteritis.
1992	3	C	M	Died	S.C.M. Kahn test +++ X-ray 'rickets fairly well marked.'	Congenital syphilis and rickets.
1999	5	C	M	Died	S.C.M. X-ray 'well-marked rickets.'	Rickets and pneumonia.

Illustrative case reports

Case 1. (To show radiological appearance compared with histological report.)

HISTORY. A Chinese male infant, aged three months, was admitted on August 16, 1939, on account of recurrent convulsions. The patient was a twin (the other twin having died at three weeks of age) and had been fed on Alpine sweetened condensed milk.

FAMILY HISTORY. Both father and mother were alive and healthy; in both cases the Wassermann reaction was negative and there was no history of venereal disease. The mother had had one miscarriage at five months, two years previously. This was the second pregnancy.

EXAMINATION ON ADMISSION. The infant was having recurrent convulsions. The weight was 6 lb. 14 oz., the temperature 98° F., the respiration rate 40, and the pulse rate 130 per minute. The knee jerks were absent. The Wassermann reaction was negative (also after provocative injection).

RADIOLOGICAL REPORT. 'Periostitis' and slight flaring of ulnar metaphysis.

PROGRESS. The infant was given vitamin B, 2000 units daily for three days, Adexolin minims 5 t.d.s., and Mead's mineral tablets 1 t.d.s. The general condition improved and the convulsions ceased, but after two weeks the infant developed pneumonia and enteritis and died.

POST-MORTEM (HISTOLOGICAL) REPORT. The rib shows well-marked widening of the zone of cartilage columns, with irregularity and distortion of the columns. Vascularity is marked. Osteoid substance is abundant. The knee shows slight irregularity of the cartilage columns. In the wrist, irregularity and distortion of the cartilage columns are present with increased vascularity, but are not as well marked as in the ribs. The osteoid substance is increased.

DIAGNOSIS. Rickets and beri-beri; terminal enteritis and pneumonia.

FIG. 1.—Case 1. 'Periostitis' and slight flaring of ulnar metaphysis.

Case 2. (To show rapid recovery with treatment.)

HISTORY. A Chinese male infant, aged eight months, was admitted June 26 to August 10, 1939. The infant had been fed on sweetened condensed milk from birth; for one week there had been fever and cough.

FAMILY HISTORY. Both parents alive and well, and in both cases the Wassermann reaction was negative. One older child, aged three years, was healthy; a second child died, aged six months; the patient was the third child.

EXAMINATION ON ADMISSION. The infant weighed 12 lb. and was flabby, cyanosed and dyspnoeic. The temperature was 101° F., the pulse extremely rapid and the respiration rate 60 per minute. The ribs were markedly beaded, and the epiphyses enlarged. The Wassermann reaction was negative (also after provocative injection).

PROGRESS. The infant was given intranasal oxygen and stimulants on admission, vitamin B, 2000 units daily for three days, and atropine. The general condition improved. The infant was

FIG. 2.—Case 2. Advanced rachitic changes (1.7.39) and progressive healing (19.7.39 and 9.8.39).

x-rayed five days after admission and then given Adexolin minims 10 t.d.s., Mead's mineral tablets 1 t.d.s., and ten treatments with ultra-violet light.

RADIOLOGICAL EXAMINATION. July 1, 1939. Severe active rickets.

July 10, 1939. Improvement.

August 9, 1939. Well-marked improvement.

DIAGNOSIS. Rickets and beri-beri; pneumonia.

Case 3. (To show typical appearance of rickets and malnutrition.)

HISTORY. A Chinese female infant, aged fourteen months, was admitted on July 26, 1939, had been fed from birth on sweetened condensed milk and 'bubo' (soft boiled rice).

FAMILY HISTORY. The father was alive and healthy; he was a coolie earning 10 to 18 S.S. dollars a month. The mother was alive and healthy

FIG. 3.—Case 3. Advanced rachitic changes.

and ate white rice. The oldest child, aged six years, and the second child, aged four years, were described as 'well'; the third child was the patient; a fourth child had died, aged one month.

EXAMINATION ON ADMISSION. The infant was emaciated, weighing 10 lb. 5 oz. The abdomen was distended; ascarides were present. The ligaments were lax, kyphosis was present, and the ribs showed very marked beading. There was no craniotabes.

PROGRESS. Treatment consisted of general measures, Mead's mineral tablets and cod liver oil; calciferol, 6 mgm., was given intramuscularly. Progress was slow, as the child's power of digestion and assimilation was seriously impaired.

RADIOLOGICAL REPORT. Advanced rachitic changes are present in all long bones, including the ribs; the bone-shadow generally is poor.

Case 4. (Early rickets and terminal pneumonia in an infant, aged 40 days.)

HISTORY. A Chinese male infant, aged 40 days, was admitted July 16 to 26, 1939. He had been fed from birth on sweetened condensed milk. Fits and pyrexia had occurred for one day. (Family history was not obtained.)

EXAMINATION ON ADMISSION. The infant was cyanosed, having frequent fits, and weighed 8 lb. 2 oz. The temperature was 99° F., the respiration rate 30, and the pulse 120 per minute. The ribs were beaded and the abdomen prominent; there was no craniotabes. The spleen and liver were not felt. The knee jerks were diminished. The Kahn test was negative.

PROGRESS. The fits were relieved by lumbar puncture and the administration of chloral. The cerebrospinal fluid was normal. The infant was treated with Adexolin minims 5 t.d.s. and Mead's

FIG. 4.—Case 3. Advanced rachitic changes at knee.

mineral tablets 1 t.d.s. He developed pneumonia and died.

RADIOLOGICAL REPORT. July 17, 1939. Slight periostitis and some rarefaction, with cupping of ulnar epiphysis.

POST-MORTEM (HISTOLOGICAL) REPORT. The rib shows slight proliferation of the cartilage columns, but the irregularity is not marked. There is increased vascularity of cartilage present with

FIG. 5.—Case 3. Beading of ribs, hypotonia, and kyphosis.

irregular downgrowths of cartilage substance into the marrow. Irregular calcification is seen, and there is an increase of osteoid substance. In the wrist, the cartilage columns show slight irregularity;

FIG. 6.—Case 4. Slight periostitis and some rarefaction, with cupping of ulnar epiphysis.

there is increased vascularity of the preparatory zone of cartilage and increase of osteoid substance, with irregular calcification. The knee shows similar appearances to those seen in the wrist.

Case 5. (Typical case of rickets: history, x-ray and histological report.)

HISTORY. A Chinese male infant, aged five months, was admitted May 6 to 31, 1939. According to the Health Nurse's card, the baby was born on December 10, 1938, and was given both the breast and tinned milk until February, 1939; after then he had sweetened condensed milk only. He was visited five times in his home and attended the welfare centre five times. In March, 1939, he was admitted to hospital for a week with 'lobar pneumonia' (during the absence of the author). He was subject to attacks of bronchitis and enteritis, and was usually found 'very dirty.' (The Chinese do not believe in washing a sick person.) In May, 1939, he was given Parrish's food and cod liver oil at the welfare centre. (Family history was not obtained.)

EXAMINATION ON ADMISSION. The infant was thin, toxic, and dehydrated, weighing 7 lb. 9 oz. The temperature was 101° F., the pulse rate 150, and the respiration rate 42 per minute. The ribs were markedly beaded; craniotabes were absent. There were signs of pneumonia at the right base. The Wassermann reaction was negative (also after provocative injection)

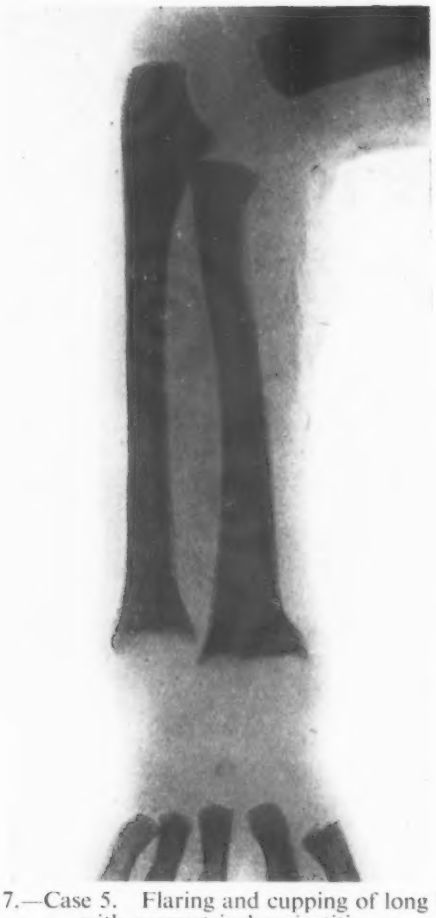

FIG. 7.—Case 5. Flaring and cupping of long bones with symmetrical periostitis.

RADIOLOGICAL EXAMINATION. Marked flaring and cupping of the ends of the long bones, and symmetrical periostitis of all the long bones.

PROGRESS. The infant was given the usual treatment, but developed diarrhoea and died.

POST-MORTEM (HISTOLOGICAL) EXAMINATION. The rib shows marked increase in depth of cartilage columns with great irregularity and distortion of these. The vascularity of the cartilage is increased and there is marked downward proliferation of cartilage substance into the marrow. Irregular areas of calcification and osteoid material are present. The wrist shows much the same picture as the ribs, except that there is no marked increase in the depths and irregularity of the cartilage columns.

Case 6. (To show advanced rachitic changes.)

HISTORY AND FAMILY HISTORY were not obtained.

EXAMINATION ON ADMISSION. A Chinese male infant, aged eleven months, appeared undernourished and extremely anaemic. The ribs were markedly beaded and a well-marked Harrison's sulcus was present. The epiphyses were enlarged; there was no craniotabes. The teeth were hypoplastic, and the limbs slightly bowed. Pneumonia was present. (The infant died after four days.)

RADIOLOGICAL EXAMINATION. Marked rachitic changes present. The bones were re-x-rayed post mortem. The accompanying figures (fig. 8 to 11) show the advanced rachitic changes, whilst the striations on the skull are similar to those seen in Cooley's anaemia.

FIG. 8.—Case 6. Skull showing striations resembling those seen in Cooley's anaemia.

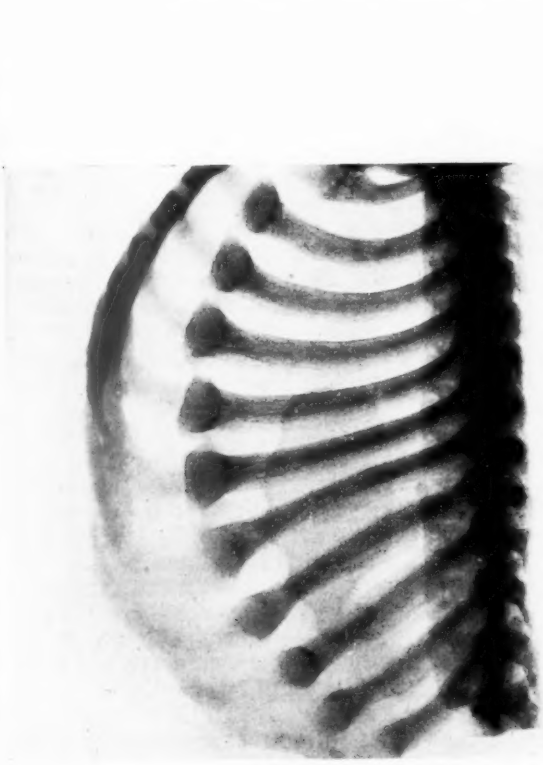

FIG. 9.

FIG. 10.

FIG. 11.

FIG. 9.—Case 6. Post-mortem x-ray of costochondral junctions showing advanced rachitic changes.
FIG. 10.—Case 6. Post-mortem x-ray of femur (rachitic changes).
FIG. 11.—Case 6. Post-mortem x-ray of tibia and fibula (rachitic changes).

CASE REPORTS

DWARFISM WITH RETINAL ATROPHY AND DEAFNESS

BY

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In 1936 I described a sister and brother under this title. At that time they were invariably good-tempered, quick in their movements, and very excitable, laughing much more readily than children of normal mentality.

Their mental and physical state has changed very considerably during the last nine years and, since no description of the condition has been found in medical literature, I think their present state should be placed on record. A more complete family history is now available and the weight of the children at birth and during the first two years of life has been obtained from the Infant Welfare Centre at Woolton Hill.

The maternal grandfather was about 5 ft. in height, the maternal grandmother taller; they had nine children, the first was a male more than 6 ft. in height, who had four children, two sons and two daughters, all big and normal; the second a female, 5 ft. high, who had a son 6 ft. high; the third a female, 5 ft. high, who had a normal son and daughter; the fourth a male nearly 6 ft. high, who had two sons and a daughter, all tall; the fifth a female, 5 ft. high with no children; the sixth a male, 4 ft. 6 in. high, who had seven children, a son, three daughters, a son, and two daughters, the second daughter being 4 ft. 6 in. and the fifth tall; the seventh child was Mrs. D., 5 ft. 1 in., whose children, the subject of the paper, will be described subsequently; the eighth child, a male, 6 ft. 4 in. high, had ten children, at least six of them boys, all rather tall; the ninth child, a male, 6 ft. high, had no children. Mrs. D. had eight children, the first three were daughters, all tall, the second being the tallest of the sibship, the fourth was a son as tall as the third daughter, then came Pearl and David, followed by a daughter, who died in infancy, followed by a son, aged thirteen, who is already taller than his mother. Mr. D., who says he is not a blood relation of his wife, was about the fifth of a sibship of nine or ten, most of whom were of average height, though one was very small and became a jockey.

PEARL D., born July 11, 1927, weighed 6 lb. 12 oz. at birth, 16 lb. 13 oz. at one year, 20 lb. at two years, and 23 lb. at three years and ten months; David D., born March 7, 1929, weighed 6 lb. 8 oz. at birth, 19 lb. at fourteen months, 21 lb. at two years, 23 lb. at three years, 26 lb. 10 oz. at four years, and 32 lb. at five years of age. Pearl D., aged 17 years 11 months, is now 3 ft. 4½ in. in height with a head 18 inches in circumference. The head appears small with abundant black silky hair. The face is very striking, prognathous with deeply sunk eyes and partial absorption of orbital fat, the nose prominent and straight, and the central incisors large. The eyeballs are sunken with occluded pupils filled with the remains of lens and capsule following an operation for discission of the lens. The corneae are clear. There are no signs of intraocular infection and the tension is normal. The palate is highly arched and the alveolar margins are thick. She is very thin, with undeveloped breasts, there is no axillary hair, but pubic hair is present. Menstruation began at thirteen years and continued regularly once a month, until she was operated on for cataract two years ago. Since then she has had only two periods, the last seven weeks ago. The feet are cold and blue even on a warm day and there are many small pigmented moles on the arms, legs, and trunk. Physical examination was difficult, but revealed no abnormality of the heart, lungs, or abdomen. The knee jerks were exaggerated and the plantar responses flexor. The hands appear unduly large; there is limited flexion at the first metacarpo-phalangeal joint of both hands, and to a slight extent at the second, but the movements of other finger joints are full; at the wrists flexion is limited, but extension is full; at the elbows there is slight limitation of extension, but flexion is full, and there is full movement of the shoulders.

The second toes are shorter than the big toes or third toes, the knees show some permanent flexion with contracture of the muscles, but movements at the hips are normal. She is quiet and sits contentedly playing with a piece of string. She can dress herself and blow her nose. She smiled when tickled, but cried when she was undressed. Blindness and deafness make it impossible to assess the degree of mental deficiency. Owing to her struggles it was impossible to carry out a complete X-ray examination of the skeleton and Dr. Kemp was dissatisfied with the X-ray of the skull. He reports that the skull bones are very thick, but could not see the outline of the pituitary fossa clearly.

Three days after admission to the hospital she had a sudden attack marked by stertorous breathing and a very rapid irregular pulse. On auscultation pulsus bigeminus was present and the beats were fluttering in character. On injection of ½ to 1 c.c. of coramin the attack ceased abruptly and the cardiac rhythm was restored to normal. The mother stated that she had had one similar attack previously,

though not so severe. When the coramin was given it was noted that there was a latent period of about three seconds before any pain response to the prick occurred and then there was a violent protest.

DAVID D., aged 16 years and 3 months, is 3 ft. 8½ in. in height with a head 19 inches in circumference. His mother stated that he went to school at 5½ years, but could not be taught anything at an ordinary school. It was discovered that he

FIG. 1.

was deaf and he was transferred to a school for the deaf at Exeter, where he began to make some progress. He then got rubella and has neither spoken nor heard much since. He has not been to school for six years. His sight was fairly good, but has been failing for six years, though he is not yet blind. On examination he appears to be intelligent, but being almost completely deaf and nearly blind, it is impossible to determine his mental level. His visual acuity is between 3/60 and 6/60. Both lenses show dense but thin opacities, which blur the picture of the fundus. The optic discs can, however, be seen and show a condition of primary optic atrophy, being dead white with very small vessels. The fundus cannot be seen well enough to make any statement about the pigmentation, which was noted ten years ago. Treatment for his eyes was tried by means of atropine, as the opacity seemed to be slightly denser in the centre of the lens than at the periphery. The pupils dilated, but visual acuity did not appear to be improved. Needling of the lens was not advised on account of the optic atrophy, which is the chief cause of his poor sight at present.

He is able to dress himself, buttoning his shirt-cuffs with one hand, and put on his shoes, tying the laces quickly and neatly. When I saw him he put one stocking on the wrong way round, but twisted it round at once. Indoors he is very fond of playing with an electric torch, but prefers to be out of doors. He is said to help his father, who is a woodcutter, using a small billhook and stacking wood. He smiled and was friendly at first, but resisted attempts to examine him, struggling, trying to pinch and kick, and weeping with rage. As soon as he was allowed to dress his violent temper passed and he became friendly again.

He is thin with medium brown hair and blue eyes, a long prominent nose and deep-set eyes. He has a high narrow palate, broad alveolar margin, and his teeth are carious. The skin is rough and dry, that on the face peeling from sunburn, and his feet are cold and blue, but not as bad as his sister's. Examination of the chest and abdomen disclosed no

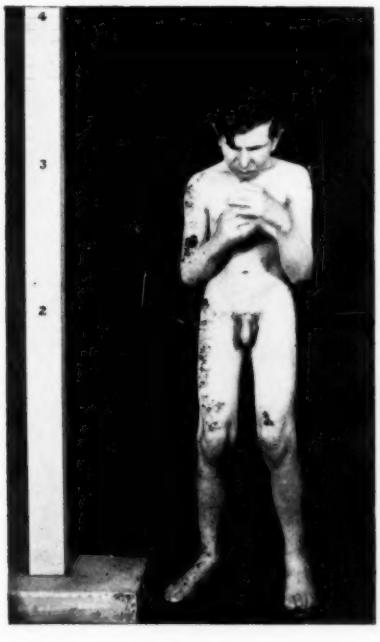

FIG. 2.

abnormality. There is no axillary hair, the pubic hair has a feminine distribution, the size of his penis is proportionate to his stature, the right testis is rather small and the left undescended. The knee

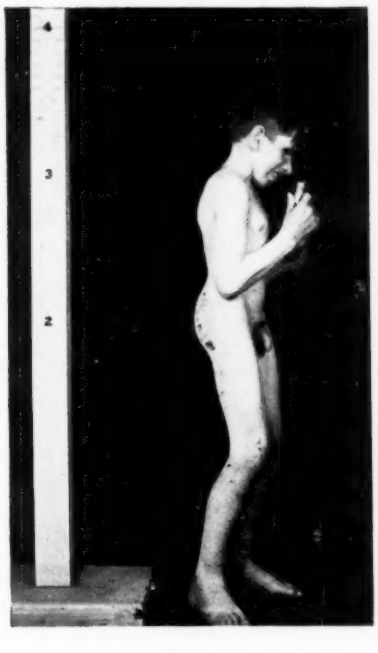

FIG. 3.

and ankle jerks are present, but it is not possible to test the plantar response. The urine is acid with a trace of protein, but no sugar, and occasional leucocytes and epithelial cells were seen. The

hands are large and the finger joints appear to be swollen. There is limited flexion of the thumbs and first fingers at the metacarpo-phalangeal joint, at the wrist extension is greatly limited, but flexion is full. The knees are slightly flexed and the right cannot be straightened owing to contracture of the muscles. The second toe of the left foot is shorter than the big toe, but the right foot is normal. Movement at the hip joints is normal. He does not walk as well as he did and is apt to stumble and fall, but this may be due to failing eyesight.

Dr. F. H. Kemp was only able to take X-rays of the hands and skull. He reports that the degree of skeletal maturity is normal for his age, and that the bones are small and the skull is very thick.

The condition, which is probably recessive, appears to be a definite entity not previously described. It is characterized by dwarfism with prognathism, thickening of the skull bones and other skeletal changes, a peculiar form of retinal pigmentation, optic atrophy, and cataract, deafness, and mental deficiency. The extremities are cold and blue. If it is possible to keep in touch with the children, it will be interesting to see whether further changes take place in later life.

I am very much indebted to Professor Ida Mann for allowing me to examine the children again and for her report on the state of their eyes, and to Dr. F. H. Kemp for taking X-rays of their skulls and hands.

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CASE OF CONGENITAL ATRESIA OF THE OESOPHAGUS WITH INFANTILE PYLORIC STENOSIS

BY

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History. A healthy white woman of 24 was delivered on October 14, 1944, of her third full term male child which weighed 5 lb. 15 oz. The infant cried promptly but was cyanosed. There was abundant mucus in the pharynx, and moist medium râles were present throughout the chest. No pyloric tumour was noted. Oxygen by nasal funnel relieved the cyanosis until the child fed, whereupon, within twenty seconds, it became deeply cyanotic, choked, and regurgitated nearly all the feeding. Hypodermoclysis with 5 per cent. glucose saline was instituted.

X-ray investigation was carried out on October 17, 1944.

1. FLUOROSCOPY. Thin barium suspension was given under the fluoroscope and was seen to fill the oesophagus to the level of the clavicle, where it collected as in a pouch, which when full contracted and expelled the barium.

2. FILMS of the thorax and abdomen after barium (fig. 1, B) show that the bronchi are outlined, and fine mottling is seen in the right and left lung fields.

Those of the abdomen show that the stomach contains gas and, in its distal portion, a dense shadow such as that caused by barium.

3. IMPRESSION. Congenital atresia of the oesophagus with tracheo-oesophageal fistula.

Progress. After consultation with the senior

FIG. 1, A.—X-ray of thorax and abdomen before ingestion of barium.

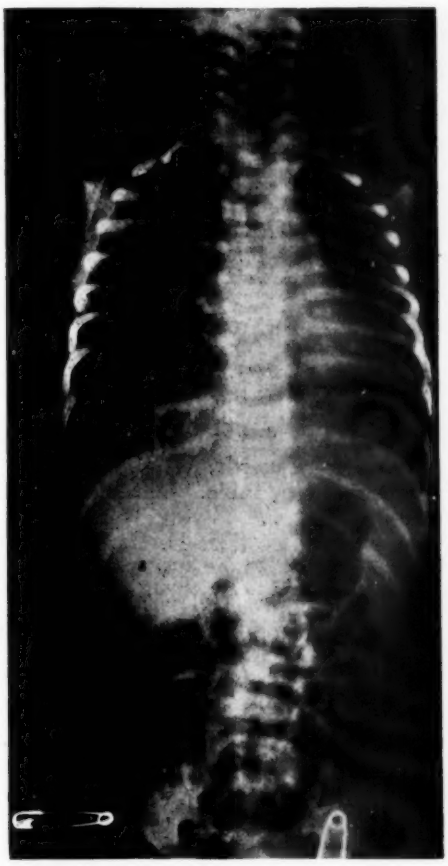
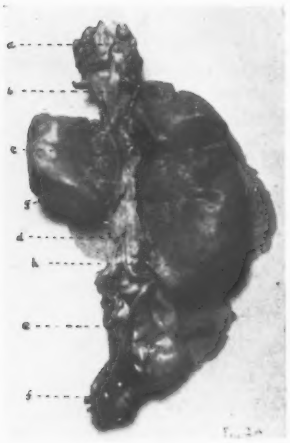


FIG. 1, B.—X-ray after ingestion of barium. (*a*) Outlined bronchi. (*b*) Fine mottling both lung fields. (*c*) Barium shadow in stomach.



A

B

FIG. 2.—Photograph of specimen.

(A) Anterior aspect. (B) Posterior aspect.

(*a*) Larynx. (*b*) Trachea. (*c*) Bifurcation of trachea. (*d*) Distal oesophagus. (*e*) Stomach. (*f*) Pylorus (hypertrophic, stenosed). (*g*) Right lung (lower portion cut away). (*h*) Left lung. (*i*) Director in oesophageal pouch (proximal oesophagus).

Bermuda surgeon, Mr. W. E. Tucker, surgery was considered inadvisable. The child died on the eighth day.

Necropsy report (Dr. R. E. Shaw). The body was that of an emaciated white male infant, aged eight days, weighing 4½ lb.

The stomach, oesophagus, lungs, trachea, larynx, heart, and great vessels were removed en masse. On opening the stomach and lower oesophagus, the latter was found to join the trachea posteriorly at its bifurcation. The trachea was otherwise normal, except that the mucous membrane had a more linear appearance where it opened into the oesophagus. The proximal portion of the oesophagus ended in a blind pouch one inch below the level of the cricoid cartilages of the larynx (fig. 2).

The lungs presented a mottled appearance, the mottling consisting of red, firm areas, some of which appeared as atelectatic spots while others were pneumonic; these red areas were scattered throughout both lungs.

The stomach was normal except at its pyloric end, where there was hypertrophy of the pylorus with consequent stenosis.

The bowel was shrunken and contained only a small amount of fluid and mucus.

The liver, pancreas, spleen, genito-urinary and osseous systems, were normal.

SUMMARY. Death was due to inanition and pneumonia due to congenital atresia of the oesophagus with tracheo-oesophageal fistula. Infantile pyloric stenosis was present.

Discussion

1. Grey Turner stated (1944):
   - (i) Congenital atresia of the oesophagus occurs once in about 2500 births;
   - (ii) Four out of 21 such cases operated upon by Cameron Haight in America recovered;
   - (iii) Operation should be performed on the first or second day of life.

2. The association of infantile pyloric stenosis with congenital atresia of the oesophagus, unless this is merely a coincidence, is important if surgical treatment of the latter is considered, since, if unrecognized, it might vitiate a successful operation.

3. The early onset of infantile pyloric stenosis in this case may possibly be related to the absence of food in the stomach, with consequent non-neutralization of the gastric juices (Engel's theory of hyperacidity).

REFERENCE

Turner, G. (1944). *Newc. med. J.*, **22**, 1.

BRITISH PAEDIATRIC ASSOCIATION

REPORT OF CHILD PSYCHOLOGY SUB-COMMITTEE

Terms of Reference. 'That the Sub-Committee should examine and inquire into the existing facilities for the diagnosis and treatment of Psychological problems in childhood, and the character of the work undertaken in such places as are provided.'

In this country psychological problems in childhood are dealt with by various organizations, the majority of which are recognized by the Child Guidance Council. In a pamphlet published by this Council in July, 1944, a list of 106 clinics is given for England and Wales and 21 for Scotland. There are in addition a few other clinics run by private organizations. These figures refer to 'clinics' and not to 'clinic teams', who may hold clinics in several different places. There are approximately 70 such 'teams' in England and Wales.

Under auspices of or attached to:	No.	Group: I	Group: II and III	Unclassified	Closed for war	At hospital but under Local Authority
Public Health Authority	53	26	2	23	2	
Education Authority ..	27	3	2	21	1	
University	1		1			
General Hospital ..	10			5	1	4
Children's Hospital ..	6			3	1	2
Neurological Hospital	3			2		1
Mental Hospital ..	1		1			
Independent Clinic ..	5	3		1	1	
Total: England and Wales	106	32	6	55	6	7
Total: Scotland ..	21	Clinics under various authorities and unclassified in report of Child Guidance Council				

Of the total number in England and Wales, about which information is readily available, only 6 clinics form part of or are attached to Children's Hospitals. About 10 are attached to General Hospitals, 3 to Neurological Hospitals and one to a Mental Hospital. Apart from these the bulk are provided and financed wholly by local authorities either of the Departments of Education or Public Health.

Types of Organization. There are three types of organization:

1. INDEPENDENT CLINIC, controlled by a voluntary committee with representatives of public bodies, educational interests, magistrates, doctors, etc. These clinics are financed by methods adopted by other 'voluntary' bodies, such as private subscriptions, sales of work, by grants from Education Committees, as well as by fees which vary according to the means of the parent.

2. THE HOSPITAL CLINIC, controlled by the hospital authorities, and attached to the Psychiatric out-patient department of a General Hospital or a Children's Hospital, or a Children's Department of a General Hospital.

3. THE LOCAL AUTHORITY CLINIC, controlled by the Local Public Health Authority or the Educational Authority, and financed entirely by them.

Each of these organizations claims certain advantages. The Independent Clinic enjoys certain freedom in carrying out general educational work and in the selection of cases; does not need to restrict itself to any area and can make its own rules for the acceptance of private cases.

The Hospital Clinic has the advantage of the co-operation of the other units of the hospital service in conducting physical examination and treatment when necessary. In addition, the parents and many of the children become accustomed to the hospital environment, but there appears to be a difference of opinion as to whether this advantage is offset in cases of nervous children by painful or frightening experiences which they have had at hospitals.

Both these types of clinics have the great disadvantage of inadequate financial aid and therefore the possibility of inadequate staffing.

The Public Authority Clinic, on the other hand, has financial stability and is in a position therefore to attract adequate and fully qualified personnel. There is also a closer association with schools and this has an advantage in cases requiring educational treatment.

Under the new Education Act it has become obligatory for the Local Authority to find out the handicapped children in its area, both physical and mental, and to provide facilities for their diagnosis and treatment. The onus for the provision of such facilities falls upon the local education authority who are guided in the setting up of clinics by the Board of Education.

The Child Guidance Council. The work of this body in this field of medicine is of such importance that a brief note about its activities and aims may serve as useful information to the members of the B.P.A. It is a constituent body of the Provisional National Council for Mental Health. It is the central body of the Child Guidance Movement and works in close liaison with the Ministries, Government departments, Medical, Social and other organizations.

The Council was formed over sixteen years ago and was supported financially by the Commonwealth Fund of America. This support lapsed in 1943. Since then the Council have had to depend on subscriptions and membership fees. They also receive a substantial grant from the Ministry of Health.

Its members are both lay and medical and include representatives from all the various Child Guidance Clinics and organizations throughout the country.

Its aims are most comprehensive and are designed to 'promote co-operation among existing bodies concerned with the treatment of children's behaviour difficulties; to increase facilities for Child Guidance work through the agency of Health, Education, and other authorities, as well as voluntary organizations, and to educate all sections of the community in the nature and value of such work; to facilitate exchange of views and co-operation between Child Guidance centres; to assist in obtaining financial and other support for Child Guidance activities; to encourage training, special study, and research into the methods of Child Guidance; to give advice and instruction in the methods of Child Guidance by means of practical courses, conferences, lectures, and other means; to commission and publish books, pamphlets, or other literature.'

The Child Guidance Council divide the various clinics into 3 groups:

GROUP I. FULL SERVICE, i.e. staffed by a full team of qualified staff, a Psychiatrist, a Psychologist and a Psychiatric Social Worker.

GROUP II. PARTIAL SERVICE.

(a) Clinic with a Psychiatrist, and either a Psychologist or a Psychiatric Social Worker.

(b) Clinic with no Psychiatrist, but with Psychologist and a Psychiatric Social Worker.

GROUP III. PARTIAL SERVICE.

(a) Clinics with a Psychiatrist, but without a Psychologist or Psychiatric Social Worker.

(b) Without a Psychiatrist, but with either a Psychologist or a Psychiatric Social Worker.

In the table above it will be seen that in England and Wales only 32 are fully staffed at present and 55 remain unclassified. This has been due to the difficulties of staffing during the war. For the same reason 6 clinics have been temporarily closed.

The Council recommend that the ideal or orthodox staff for a Child Guidance Clinic run either as part of any hospital or as a separate entity, should be composed of a Psychiatrist, a part-time Psychologist, and a full-time Psychiatric Worker. They define the qualifications for such a staff as follows :—

CHILD PSYCHIATRIST. In the absence of any recognized Diploma or qualification it is difficult to define, but in general terms he or she should possess a medical qualification and a Diploma in Psychological Medicine. He should have training in dealing with the psychoneurosis of adults, experience with sick children and of normal children, and special training in Child Guidance. A personal analysis is thought to be desirable.

The Psychiatrist should be the Director of the clinic and should devote a minimum of two sessions of 2½ hours a week at each clinic to which he is attached. In addition to the general direction of the clinic it is his task to diagnose the case and recommend the treatment to be followed.

A CHILD PSYCHOLOGIST should have an Honours degree in Psychology (or its equivalent), experience with children in teaching and other work, a knowledge of educational methods followed by training in Intelligence testing, and Child Guidance team work in a clinic.

The duties include mental testing, individual coaching to children who have fallen behind in school from other causes than lack of intelligence, and dealing with other educational problems arising in schools. He or she should attend at least two half-sessions a week at each clinic and be salaried.

A PSYCHIATRIC SOCIAL WORKER, besides having a Diploma in Social Science and experience in general social work, should have the Mental Health Certificate of the London School of Economics. She should be a full-time member of the staff of the clinic and be salaried.

The duties include the interviewing of parents, home visiting, co-ordinating adjustment between home, school and clinic, and securing the co-operation of other departments and agencies.

In addition, Play Therapists and Speech Therapists may be employed if necessary.

Equipment and Premises. The premises should be, but rarely are, adequate and should consist of at least: One or two clinic rooms, one waiting-room, one room for Psychologist, one room for Psychiatric Social Worker, one office, and one or two playrooms.

The equipment and furniture should be such as would make it attractive to children with play material and toys, and as little like a formal office as possible. A garden would be an advantage.

Finance of Clinic. This will vary with the size of the school population to be served, the size of the geographical area served, and the composition of the team. In the case of clinics attached to teaching hospitals the Psychiatrist may work in a voluntary capacity.

With a full team of paid personnel serving a school population of say 20,000 children and dealing with about 200 cases a year the following estimate has been made by the Child Guidance Council:

	£	s.	d.
THE PSYCHIATRIST attending 4 sessions per week at 2½ guineas to 3 guineas per session, say	525	0	0
PSYCHOLOGIST attending half time for clinic and half time for Education Authority	450	0	0
PSYCHIATRIC SOCIAL WORKER. Full-time salary of £300 to £500 a year according to experience, say	360	0	0
CLERICAL ASSISTANT. Full-time salary, say	150	0	0
Total	1,485	0	0

It will be appreciated that for many of the Independent and Hospital clinics the above estimate creates a heavy financial burden. The expense has been met to some extent by charging fees. This may be paid by the parents or by the local authority if the child is seen on their behalf. The usual fee of 15*s.* for a diagnostic interview and 5*s.* for each subsequent treatment has been inadequate and the matter has recently been under consideration with the result that the fees now recommended show a substantial increase to cover salaries of personnel and overhead expenses.

A. DIAGNOSTIC INTERVIEWS—

(1) FOR FULL EXAMINATION:

	£	s.	d.
Salaries	1	10	0
Overheads ..		12	0
	2	2	0

(2) FOR PARTIAL EXAMINATION:

	£	s.	d.
Salaries		15	0
Overheads ..		6	0
	1	1	0

B. TREATMENT INTERVIEWS—

(1) FULL SERVICE:

	£	s.	d.
Salaries		16	6
Overheads ..		4	6
	1	1	0

(2) PARTIAL SERVICES: 10 6

These estimates are for individual examination and treatment. They are based on the consideration that the time spent for diagnostic interviews is an hour for each worker concerned (this has to include discussion, reports, letters, etc.). For treatment interviews a shorter time (approximately 40 to 45 min.) per case is allowed.

In those clinics set up by the Local Education Committee, the Board of Education give a grant up to 50 per cent. of the cost if the clinic is adequately staffed. The remaining cost falls on the rates.

Character of the work done. Cases are referred to the clinics from various sources: private doctors, school medical officers, teachers, parents, social agencies, magistrates, probation officers, etc. Children of all ages are accepted and in some clinics up to 18 years old. The problems dealt with include anxieties and fears, sleep disturbances, temper outbursts, stammering, enuresis, truanting, educational retardation, delinquencies such as stealing, sex offences, persistent lying, etc., psychological symptoms in physical disorders and physical symptoms in psychological disorders.

The work done includes diagnostic consultation and treatment. It is impossible to outline any definite pattern of the nature of the work at the various clinics, but in a fully staffed clinic each case is studied separately by each member of the team and their opinions pooled before making a diagnosis or deciding on the treatment to be followed.

The treatment will depend on the type of problem and includes psychotherapy in appropriate cases; remedial teaching when the difficulty is an educational problem; adjustment of environmental conditions when necessary; or selection of more favourable environment for children constitutionally handicapped whether intellectually or emotionally. In this last connection accommodation can be obtained for many of these maladjusted children in hostels approved by the Ministry of Health. There are at present about eleven such places. In some, education is provided on the premises. In others the children attend the local schools.

Cases for treatment will be limited qualitatively and quantitatively to the type of case commonest to the clinic's natural clientele. For example, the Hospital Child Guidance Clinic will provide many psychosomatic problems besides failure of adaptation in home and school life, and intellectual difficulties.

Clinics associated with school services will receive a predominant number of educational facilities.

Mentally deficient children are not the concern of Child Guidance Clinics and are transferred to the appropriate authority when diagnosed.

In the case of delinquent children there are no special facilities apart from that provided by the Institute for the Scientific Treatment of Delinquency, and many, unless they need supervision in an approved school, attend the ordinary clinics for treatment.

The big demand on Child Guidance Clinics for diagnostic examination makes it essential that the psychiatrist, basing his views on the reports of his staff or team, will alone be responsible for deciding which cases are to continue their attendance at the clinic. A suggestion is that at a big clinic the Psychiatrist should collect the case reports referred each week and select from them those children suitable, returning the others. When children present simple problems of a psychosomatic nature the Psychiatrist should make a diagnosis and then send the child back to the Paediatrician with his reasons for the diagnosis and suggestions for treatment.

The basis upon which the patients in a teaching hospital are referred to the Children's Psychiatric Clinic in that hospital must remain largely a matter of mutual education and arrangement between the Paediatricians and the Psychiatrists.

Physical aspect. It is accepted by all engaged in this work that at every clinic arrangements should be made to ensure that each child receives a general physical examination by a competent physician.

The procedure in this respect varies widely. In the case of teaching hospitals and children's hospitals a Paediatrician is available. In others a Paediatrician may be attached to a clinic. In many others the physical examination is undertaken by the School Medical Officer. In some the Psychiatrist has a definite interest in Paediatrics and undertakes the investigation of the physical condition himself.

Case load. At the present time there do not appear to be sufficient clinics to meet the demands. It is estimated that about 1 per cent. of the child population requires help at a psychiatric clinic. (The child population at present is about 4½ million.)

A full-time clinic fully staffed could deal with a child population of about 40,000, providing approximately 400 cases a year. This means not more than 8 new cases a week.

Training of Child Psychiatrists. During the past few years there has been an ever-increasing number of Child Guidance Clinics. As has been pointed out above, the new Education Act compels the Local Authority to provide adequate facilities for the diagnosis and treatment of psychological disorders in children. In order to meet this demand many more clinics will be started.

There is, however, a great dearth of trained Child Psychiatrists at the present time and with the anticipated expansion of the service the shortage will be all the more acute.

The Sub-Committee deplore the setting up by Borough Councils and Education Authorities of so-called Child Guidance Clinics under the control of either an Educational Psychologist or a Psychiatric Social Worker working alone. (N.B. It has been suggested by a member of the Board of Education, however, that for many of the clinics, especially when educational problems form the bulk of the work, it is better, until more trained Psychiatrists are available, to have a partial staff than none at all.)

It is obvious that the need for fully trained Psychiatrists with special knowledge of children's work and with qualifications to fit them for honorary appointments on hospital staffs or as heads of Child Guidance teams is one of great urgency. In order to ensure a high standard of personnel the Child Guidance Council recognizes no training other than its Fellowship training for Child Psychiatrists, or its equivalent (such as Fripp Fellowship at Guy's, or a Rockefeller at certain clinics in the U.S.A.).

Before granting a Fellowship the Medical Sub-Committee of the Child Guidance Council have made the following recommendations:

A. Before considering an application for a fellowship certain prerequisites are essential:

(1) A Medical qualification.
(2) The D.P.M. or equivalent Mental Hospital experience.
(3) Experience with normal children and with sick children in hospital, or in general practice.

B. THE TRAINING to consist of one year's half-time work for senior candidates, and for less experienced candidates an additional one year's full-time clinical work under supervision.

The candidate must also have had experience in treatment of adult psychoneurosis, either before beginning the training or running concurrently with it.

In order to ensure that candidates should be suitable for such work the Council not only make a careful selection but reserve the right to terminate a Fellowship if the candidate is found, after a probationary period, to be unsuitable.

Such Fellowships for training are tenable at the following Institutions:

Aberdeen Child Guidance Clinic.
Bristol Education Committee Child Guidance Clinic.
Child Guidance Training Centre, Muswell Hill.
Guy's Hospital.
Hertfordshire County Child Guidance Clinic, St. Albans.
Maudsley Hospital Child Guidance Clinic.
Tavistock Clinic.
Manchester Education Committee Child Guidance Clinic.

For the full two years' course no fees are payable and an honorarium of £250 is paid in the second year. To assist Fellows during training loans up to £150 are available, and in exceptional cases grants may be given.

The place of child psychology in the training of doctors.

(a) It is false to attempt to draw a hard and fast line between physical and psychological disabilities.

(b) Without a study of both the normal and abnormal child, adult neurosis and psychosis cannot be understood.

The attendance of students at Child Guidance Clinics raises certain problems. The unqualified student should not be allowed to attend regularly the sessions of the clinic. Groups of unqualified students should, on certain occasions, be led through the clinic and the scope of the work explained to them. They have neither the time in their clinical period to absorb the special information to be derived from the clinic, nor should the work be regarded as a pre-qualification study. Their presence at the regular sessions of the clinic is likely to embarrass work.

Provision must be made, however, for students who are medically qualified and wish to learn the work of either the Psychiatrist or the Psychologist in a Child Guidance Clinic. What provision is made for such Post-Graduate students will vary from clinic to clinic with the personality of the Director. Accommodation must be available for them to observe fully all the work going on and, in their later stages of training, to undertake, under suitable supervision, the more simple parts of it.

Recommendations

1. It is a common experience of every Paediatrician to deal with many of the more simple psychological problems in children under his care. With his complete understanding of children and the confidence he shares with his patients and their parents, no one is better fitted to advise about the management and general care which these children require. Other children with a more profound psychological disorder must be referred to a Psychiatrist. A Paediatrician has not the special training required to deal with this type of patient.

2. To encourage a deeper interest by Paediatricians in the problems of child psychology, it is hoped that there will be a much closer co-operation between Paediatricians and Psychiatrists than has existed hitherto.

3. In order to foster such co-operation it is recommended that the B.P.A. should ask to have direct representation on the Child Guidance Council so that problems common to both parties might have joint attention.

4. The recommendation of the Medical Sub-Committee of the Child Guidance Council that Child Psychiatrists should have had experience with normal children and with sick children in hospital or in general practice is welcomed, but the Executive Committee of the B.P.A. recommend that this experience should be sufficiently thorough to enable candidates to qualify for the D.C.H. or some higher qualification in Child Health.

5. It is also recommended that a Child Psychiatrist attached to a Children's Hospital or a General Hospital should be recognized as a full member of the hospital staff, subject to the individual holding the usual higher qualifications.

6. The Executive Committee of the B.P.A. recommend that in Child Guidance Clinics not attached to a Children's Hospital or a Children's Department of a General Hospital, there should be available a paediatric service for physical examination of children attending such clinics wherever possible.

W. G. WYLLIE (Chairman).
CHARLES HARRIS.
Jan., 1946. C. T. POTTER.

REVIEWS

The Premature Baby. By V. MARY CROSSE, M.D. (London), D.P.H., M.M.S.A., D.R.C.O.G., Chief Obstetric Officer in charge of City of Birmingham Maternity Homes and Premature Baby Unit; Deputy Senior Assistant Medical Officer of Health (for Maternity and Child Welfare), City of Birmingham. With a foreword by Leonard G. Parsons, M.D., F.R.C.P., F.R.C.O.G., Professor of Children's Diseases, University of Birmingham. London: J. and A. Churchill, Ltd. 1945. Pp. 156, 14 illustrations. Price 10*s*. 6*d*.

This little book, the value of which is much greater than its modest size might suggest, comes at an opportune time. The concern that is generally felt over the birth rate is coupled with a realization that whilst the mortality of infants aged one to twelve months has fallen remarkably during the present century, the neonatal mortality has not been reduced to a corresponding extent. Of the infants who die in the first month, over 50 per cent. are premature. Dr. Crosse has not only had unrivalled experience in this country in the care of prematures, but over a period of years has worked out a technique of care and management which has proved its value by the results achieved. It is with this aspect of prematurity that her book is primarily concerned. Like all books based on extensive practical experience and a critical assessment of results, it should prove of very great value to those faced with similar problems. It would have been interesting to have had a more detailed follow-up of the premature infants who survived, but a sufficient number of studies have been made along these lines to establish the fact that, despite the complications and disabilities that are observed in a certain proportion of cases, premature babies are, as a group, worth saving. It is fortunate that Dr. Crosse's experience in this work is now available to a wider public.

Mitchell-Nelson's Textbook of Pediatrics. Edited by WALDO E. NELSON, M.D., Professor of Pediatrics, Temple University School of Medicine. With the collaboration of forty-nine contributors. Fourth edition, revised. Philadelphia and London: W. B. Saunders Co. 1945. Pp. 1350, 519 illustrations. Price 50*s*.

It is always a pleasure to meet old friends in new clothes, and those who have been familiar for many years, first with Dr. Griffiths' classical textbook, and later with 'Griffith-Mitchell', will now welcome the fourth edition of one of the great American paediatric texts under the editorship of Professor Nelson. The present editor was closely associated with Dr. Mitchell, whose death within a month of that of Dr. Griffith was a great loss to paediatrics, and it will be generally agreed that the task of editorship could not have passed into more suitable hands. The present edition has been entirely re-written, but whilst it is in this sense a new book, it carries on the tradition of scholarship that was a hall-mark of the previous editions. It continues to be of outstanding value as a book of reference, not only on account of the text itself but because no other one-volume paediatric text provides such a comprehensive bibliography. If the size of the team of contributors has resulted in some unevenness, it is more than compensated for by the freshness of outlook and the number of schools represented. The editor is the more to be congratulated on his success in avoiding overlapping and on the production of a text of which the standard is so high throughout.

On the technical side, the production is excellent, and if one is at first inclined to regret the double-columns and reduction of margins, it will be realized that it is only by such means that the text could have been kept within the confines of a single volume. Whilst the book may prove too formidable in size for any but the more ambitious student during his period of paediatric clerking, it is one which any doctor requiring a reference work on this subject will find invaluable.

Pediatric X-ray Diagnosis. By JOHN CAFFEY, A.B., M.D. Chicago: The Year Book Publishers, Inc. 1945. Pp. xxii and 838, Fig. 710. Price $12.50.

Dr. Caffey's reputation in the field of radiology is well established, and it will be enhanced by this new volume. It is unique in presenting up-to-date views, beautifully illustrated, on all aspects of the use of X-ray photography in the diagnosis of disease in childhood. It appears to originate from a series of conferences at the Babies Hospital, New York, over the last twenty years, and it will be seen that Dr. Caffey has been as well served by his clinical colleagues as he has served them. Six main sections cover the anatomical divisions of the body. Line drawings are used as well as X-ray pictures to illustrate the book, the whole standard of which, from the production side, is excellent. This will be a most valuable work of reference for all concerned in the care of children.

Opera Paediatrica. Edited by I. JUNDELL, A. LICHTENSTEIN, and A. WALLGREN. Uppsala (also published as **Acta Paediatrica**, Vol. XXXII, Fasc. 3–4). 1945. Pp. 629. (Price not stated.)

This volume is a splendid memorial to a hundred years of paediatric teaching and practice in Sweden, and it is fittingly associated with the names of Professors Jundell, Lichtenstein, and Wallgren, who have themselves done so much to build up the international reputation both of Swedish paediatrics and of the Acta Paediatrica. There are some fifty-two contributions, the great majority being in English, dealing with a wide variety of subjects. As would be expected, a number of these are historical. Professor Lichtenstein's 'Outline of the history of paediatrics in Sweden' and Professor Wallgren's 'Social welfare of Swedish children, past and present' will be of particular interest to English readers, in showing the way in which many similar problems to those existing in this country have been met. One cannot fail to be impressed with the similarity of outlook and ideals that have actuated paediatricians in Sweden and in Britain, and whilst we have much to learn in the applications of social medicine of childhood from our Swedish colleagues, we can feel sure that a resumption of the exchange of ideas, and personal contacts, which was so pleasant a feature of the pre-war years, will be mutually appreciated.